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MRL (DRG) REPORT NO. 3

A STUDY OF SHORT INTERVAL EXPOSURES OF GOATS TO CG, CK, AND AC.

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MRL (DPG) REPORT NO. 3
Project A 10.2

Medical Division, OC-CWS Project Specification 86

(1)

A STUDY OF SHORT INTERVAL EXPOSURES OF GOATS TO CG, CK, AND AC

by

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MEDICAL RESEARCH LABORATORY
MEDICAL DIVISION, OFFICE OF THE CHIEF, CWS
Dugway Proving Ground, Tooele, Utah

A STUDY OF SHORT INTERVAL EXPOSURES OF GOATS TO CG, CK, AND AC

Project A 10.2 MRL (DPG) Report No. 3

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ABSTRACT

MRL (DPG) REPORT NO. 3

OBJECT.

To determine the toxicity of CG, CK, and AC to goats and the respiratory behavior of goats when exposed for short periods, in order to calibrate this animal for use in field studies of surprise effects.

RESULTS.

1. Exposures of "masked" goats to CG concentrations of 1.3 to 50 mg./l. caused breath holding for 15 to 139 seconds while concentrations as low as 0.6 mg./l. caused respiratory depression.

2. Thirty second total exposures of goats to CG resulted in greater than 50% mortality only in the range of 10,000 to 12,000 mg.min./m^3. Above this range the mortality probit showed a reverse trend. This phenomenon is accounted for by breath holding at very high concentrations.

3. Exposures of "masked" goats to CK in concentrations of 2 to 50 mg./l. resulted in marked respiratory depression followed by stimulation, and, in the case of casualty doses, another period of depressed breathing.

4. The respiratory response of "masked" goats to AC was characterized by a progressive onset of stimulated breathing followed by a marked depression of breathing. Very high concentrations (20 to 45 mg./l.) caused an initial respiratory depression.

5. The L(Ct)50's for the total exposures of unmasked goats were determined as follow:

CG (30 seconds) Indeterminate (See 2. above)
CG (2 minutes) 6500 ± 750 mg.min./m^3
CK (2 minutes) 7000 ± 750 mg.min./m^3
AC (30 seconds) 1300 mg.min./m^3

6. The approximate L(Ct)50's for exposures of goats wearing special masks* were estimated as follow:

CG (t variable; average 100 seconds) 17,000 mg.min./m^3
CK (2 minutes) 14,000 mg.min./m^3
AC (15 seconds) 6,000 mg.min./m^3
AC (30 seconds) 3,000 mg.min./m^3
AC (2 minutes) 4,000 mg.min./m^3

Thirty second exposures to CG and CK showed no correlation between the concentration and mortality.

* without canister

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CONCLUSIONS.

1. The toxicity of nonpersistent agents during short exposures is largely dependent on the respiratory response of the subject during exposure.

2. Exposures to high concentrations of the irritant gases, CG and CK, result in reflex respiratory depression. This respiratory depression reduces the effectiveness of crash concentrations of these agents for surprise effects.

3. On the basis of physiological response, AC is the most desirable standard nonpersistent agent for surprise effects.

4. Short interval exposures of "masked" goats to nonpersistent gas could be subject to the following limitations:

a. The effectiveness of the agent is reduced approximately one-half by the presence of the mask under the conditions tested.

b. The dead space of the mask dilutes the agent, unless measures are taken to circulate the atmosphere through the mask.

c. Exposures to irritant gases of two minute duration or less result in marked variation in response.

d. Exposures to irritant gases of 30 second duration or less show no correlation between the concentration of agent and mortality.

RECOMMENDATIONS.

1. Field requirements for nonpersistent agents should be re-examined in the light of these results to establish new criteria for lethal surprise effects.

2. New methods for controlled short exposures of goats in the field to nonpersistent agents should be investigated.

3. Field data obtained with unmasked and "masked" goats should be re-evaluated.

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GLOSSARY

1. Breath holding: Total cessation of respiration for a finite interval.

2. Dead space: The space in the goat mask between the nose of the goat and the inlet and outlet valves.

3. Masked goat: A goat wearing a special goat mask facepiece without a canister.

4. Probit: A statistical unit such that "0 of the usual statistical table of deviates has been equated to the digit 5 and the deviate of the normal curve in terms of 'σ' added algebraically to secure the probit corresponding to each percentage kill" (C.I. Bliss, Ann Applied Biol. 22 134 (35)).

5. Respiratory depression: Diminution of the amplitude of the respiratory excursion and/or the rate of respiration.

6. Respiratory minute volume: Volume of air respired over an interval of one minute.

7. Respiratory stimulation: Acceleration of the rate and/or increase in the amplitude of the respiratory excursion.

8. Surprise effect: Effective exposure during the period before a soldier adjusts his mask.

9. Short interval exposures: Exposures of two minutes duration or less.

10. Agents: CG - Phosgene
CK - Cyanogen Chloride
AC - Hydrocyanic Acid

11. Reference abbreviations:

D.P.G. - Dugway Proving Ground
E.A.M.R.D. - Edgewood Arsenal Medical Research Division
E.A.T.R. - Edgewood Arsenal Technical Report
M.R.L. (E.A.) - Medical Research Laboratory (Edgewood Arsenal)
N.D.R.C. - National Defense Research Committee
O.S.R.D. - Office for Scientific Research and Development
P.C.S. - Project Coordination Staff, Edgewood Arsenal
P.R. - Porton Report
T.C. - Training Circular
T.D.M.R. - Technical Division (Edgewood Arsenal)Memorandum Report
T.R.L.R. - Toxicological Research Laboratory (Edgewood Arsenal) Report
U.C.T.L. - University of Chicago Toxicity Laboratory
U.S.C.W. - U.S. Chemical Warfare Service

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MEDICAL RESEARCH LABORATORY
MEDICAL DIVISION, OFFICE OF THE CHIEF, CWS
Dugway Proving Ground, Tooele, Utah

A STUDY OF SHORT INTERVAL EXPOSURES OF GOATS TO CG, CK, AND AC

MRL (DPG) REPORT NO. 3

I. INTRODUCTION.

A. Object.

To determine the toxicity of CG, CK, and AC to goats and the respiratory behavior of goats when exposed for short periods, in order to calibrate this animal for use in field studies of surprise effects.

B. Authority.

1. CWS Project Program A 10.2 "Toxicity Determinations".

2. Medical Division Project Specification No. 86, "Bio-assay of Surprise Effects of Clouds Released from Munitions Charged with Non-persistent Agents".

II. HISTORICAL.

A. General.

In the tactical use of nonpersistent agents emphasis has been placed on the use of crash concentrations to attain surprise effects within two minutes. (U.S.C.W. Conference 102, OC-CWS; PCS Report No. 9, 17 May 1945; D.P.G. M.R. No. 21). Toward this end chemical warfare tactics have been developed for the use of such weapons as the 7.2" chemical rocket, the 4.2" mortar, and large capacity aircraft bombs. Estimates of munition requirements have emphasized 30 second to 2 minute exposures (P.C.S. Report No. 9), (T.C. 20, 26 April 1945).

In field trials of these weapons at Dugway Proving Ground, the assessment of surprise effects has been carried out by means of short interval chemical sampling and by corresponding short interval exposures of specially"masked"goats. Thirty second and two minute exposures were controlled by a remotely operated canister-bypass solenoid valve which was designed to permit an exposure of the goat to the gas cloud during the desired interval. (D.P.G. Weekly Report Series 2 - Report 83 - Part B). This apparatus was termed the "surprise" mask because of its application to the study of surprise effects. The results of the bio-assay obtained in the 7.2" chemical rocket trials of CG were erratic, particularly for 30 second exposures, and showed poor correlation with chemical data. (D.P.G. Weekly Report, Series 2 - Report 85, 86, Part B). In view of these results, and since published data on toxicity of the nonpersistent agents for goats was limited by the small numbers of animals used, a careful study of the

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physiological effects of short interval exposures to these agents was undertaken. During these studies it became apparent that a study of the respiratory response of the goats was also necessary to explain completely the toxicity for short exposures.

B. Toxicity of the Agents to Goats.

The available data on the toxicity of short exposures of CG, CK, and AC for goats are given in Table I.

TABLE I

Agent	Time of Exposure	Degree of Toxicity	Ct mg.min./m³	No. Goats Used	Source of Data
CG	1-10 Min.	L(Ct)40-80*	>4,400(2)	14	E.A.M.R.D. 5
CG	2 Min.	L(Ct)50	4,600	14	T.R.L.R. 20
CG	2 Min.	L(Ct)50*	>7,000	6	P.R. 976
CG	3 Min.	L(Ct)100*	6,600	8	Marshall(1)
CK	1 Min.	L(Ct)50*	4,500	4	P.R. 2603
CK	2 Min.	L(Ct)100*	5,000(2)	6	Suffield Report No. 71
CK	2 Min.	L(Ct)50	3,600	30	T.R.L.R. 26
CK	3 Min.	L(Ct)50*	6,000	6	P.R. 2603
AC	30 Sec.	L(Ct)100*	2,900	10	O.S.R.D. 1432
AC	30 Sec.	2/4 Mortality	4,850	4	P.R. 2298
AC	2 Min.	L(Ct)50	2,200	14	T.R.L.R. 23
AC	2 Min.	L(Ct)50*	5,000	5	P.R. 2298
AC	3 Min.	L(Ct)50	3,000	32	T.R.L.R. 23 (Summary of previous data)

Notes (1) From Winternitz, M.C., "Pathology of War Gas Poisoning", Yale University Press, New Haven, Conn. 1920
(2) Estimated from field exposures
* Estimated value

C. Physiological Effects of the Agents.

1. CG.

A recent paper (O.S.R.D. 4637) reviews the literature and presents original experimental data. Included are the L(Ct)50 values for various laboratory animals (but not including the goat), physiological effects of the agent on the lungs, the effect of temperature and other variables. Studies of the reactions of dogs exposed to CG (N.D.R.C. Monthly Progress Report 9-4-1-14, 10 March 1944) have shown that respiratory inhibition of 10 to 30 seconds duration occurred in anesthetized dogs when

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exposed to CG concentrations of 1.0 to 10.2 mg./l. Respiration returned to normal during the remainder of the one minute exposure. It was also found that during a one minute exposure dogs may be expected to breath 50 per cent of the calculated Ct, and 83 to 90 per cent during a 3 to 5 minute exposure. Rabbits and sheep, (Porton Report 2555) showed apnea on exposure to the agent, and horses reduced their breathing for one to two minutes when exposed to concentrations of 0.35 mg./l. of the agent.

Respiratory studies on anesthetized dogs exposed through a tracheal cannula for one minute to CG concentrations greater than 7.0 mg./l. showed the average reduction of the minute lung output was 62 per cent (O.S.R.D. 4637). In all except one test the first inhalation caused complete cessation of breathing with the lungs in the deflated stage. Apnea continued for 14 to 52 seconds and averaged 26 seconds. It was also shown that, following vagotomy, respiratory inhibition did not occur even though the dogs were exposed to 23.8 mg./l. Atropine, however, did not abolish the reflex. A concentration of 1.0 mg./l. caused 22 per cent respiratory reduction in anesthetized dogs during the first minute of exposure, and respiration was somewhat stimulated during the fifth minute of exposure.

2. CK.

Previous work on the toxicity of CK to various laboratory animals, exclusive of the goat, has been summarized (O.S.R.D. 5001). Data was presented on the $L(Ct)50$ values, pathology, and symptomatology. Original studies were made on the residual effects of CK on dogs and monkeys, the effect of repeated exposures on mice and dogs, and the toxicity of AC-CK mixtures.

The pathology of CK (Medical Division Report No. 34) and studies of its specific toxic activity have been presented(U.C.T.L. Informal Monthly Report N.S. 1, 15 April 1945). Detoxication by man was estimated to proceed at such a rate that 0.315 mg./l. could be inhaled indefinitely (E.A.T.R. 360). Detoxication by goats was estimated to be approximately 0.15 mg./l. (T.D.M.R. 638).

Respiratory depression during exposure to CK was demonstrated by Short and Watt (P.R. 2603), Coon (O.S.R.D. 5001), and Silver (E.A.T.R. 360). Respiratory stimulation was shown to follow respiratory depression (P.R. 2661). In field tests with rabbits at Dugway Proving Ground erratic results were obtained on the toxicity of the agent. These results have been attributed to reflex respiratory inhibition (DPG Weekly Report 54, Series 2, 3 May 1944).

Eight dogs, totally exposed to CK for 15 seconds, in concentrations of 46.7 to 50.3 mg./l. (nominal) survived. Six of these showed no symptoms at any time. Two of seven dogs exposed to CK for 30 seconds in concentrations of 41.4 to 47.9 mg./l. (nominal) survived. Five dogs exposed to CK for one minute to concentrations of 41.6 to 55.3 mg./l. (nominal) died. (Medical Division Informal Monthly Report, May 1945).

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3. AC.

Experimental studies on the toxicity of AC to various laboratory animals including the goat have been fully summarized by Coon et al (O.S.R.D. 1432, 13 April 1943). The stimulation of respiration by injection of AC and NaCN has long been known; a similar reaction following inhalation has been described in the literature (M.R.L. (EA) 15, T.D.M.R. 471, and T.D.M.R. 430). Respiratory depression following stimulation was described in T.P.L.R. 15. The time for the occurrence of convulsions was shown in T.R.L.R. 23, and that this reaction was related to concentration in T.D.M.R. 698. It has been reported that goats were able to detoxify the agent continuously when the concentration was 0.05 (O.S.R.D. 1432) and 0.10 mg./l. (T.R.L.R. 23).

4. Summary.

CG and CK in the concentrations required for lethal surprise effects have been observed to produce depression of respiration. With phosgene this depression was abolished by vagotomy and may be therefore presumed to be reflex in nature. AC and CK after the depression period, were found to produce respiratory stimulation within the surprise period. The data further demonstrated that for exposures of 2 minutes or less detoxication of AC and CK could be safely neglected. The reported data, for the most part, did not include an evaluation of the goat, and the studies, involving only small numbers of animals, did not warrant an extrapolation to field requirements. It was clear, with regard to AC, CK, and CG, that 1) the "Ct" requirement for surprise lethal effects differed in each case to an important degree from the requirement for prolonged exposures, and 2) that this difference could not be predicted from the reported data.

III. EXPERIMENTAL.

A. Materials and Equipment.

1. Dynamic flow gassing chamber (1150 liter volume)

2. Atomizers

3. Modified experimental goat mask

4. CG, CK, and AC

5. Recording tambour

6. Sampling and analytical equipment

7. Motoair vacuum pump (capacity 35 liters per minute at one-half atmosphere).

a. The dynamic flow gassing chamber (Plate 3) has a roller equipped carrier on which three goats may be placed and introduced into

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the chamber for given exposure periods. The time of exposure can be controlled accurately within plus or minus one second. The chamber pumps have a maximum capacity of 3100 liters per minute (ca. 3 chamber volumes per minute). The inner walls of the chamber are porcelain coated and all metal parts are of stainless steel. Ports are available on the sides for introduction of agent and sampling. Glass windows permit observation during the exposures. The chamber is installed in a room equipped for rapid removal of toxic vapors from its atmosphere.

b. The agents, CG, CK, and AC were dispersed from atomizers of various sizes employing a stream of nitrogen over a capillary tip (Plate 2). The atomizer was fitted into a glass flask containing a weighed quantity of liquid agent. An ice-water bath was used to cool the agent during the dispersion of CG and CK, but with AC this measure was unnecessary. The concentration of agent in the chamber was controlled by: 1) the rate of nitrogen flow through the atomizer, 2) the size of the atomizer, and 3) the chamber flow rate.

c. A goat mask developed in this laboratory for controlled field exposures was modified for the respiratory studies (Plates 1, 4). The mask consists of a metal nose piece held in position by straps around the goat's head. Two rubber diaphragms within the nose piece insure a tight fit and still permit free nasal breathing. The goat, however, cannot open his mouth while wearing the mask. A vacuum pump drawing 30 to 34 liters of air per minute was connected to the mask. An outlet valve, a tube (1 inch in diameter and 12 inches in length) fitted with an inlet valve, and pressure tubing leading to a tambour for recording breathing were all attached to the nose piece.

d. The CG and AC used were standard CW fillings obtained from the Toxic Gas Yard, Dugway Proving Ground. CK was obtained from lots of CK under surveillance at Dugway Proving Ground and known to be of high purity.

B. Animals.

380 Angora goats - These animals weighed between 55 and 110 pounds with an average of 80 pounds. They were obtained from southern Utah and normally lived at altitudes from 8,000 to 10,000 feet. Hemoglobin values for the herd averaged about 9.0 gm. per 100 cc blood with a range of 7.0 to 11.0 grams.

C. Methods.

1. L(Ct)50 Determinations for Short Exposures.

Total exposures of unmasked goats were made in the dynamic flow gassing chamber in order to determine the L(Ct)50 for 30 second and 2 minute exposures to CG, 2 minute exposures to CK, and 30 second exposures to AC. Goats were exposed in groups of either two or three for the desired period. The chamber was operated at 1 to 3 chamber volumes per minute and

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at least 5 minutes were allowed before exposures to permit the chamber to reach equilibrium. Samples of the chamber atmosphere were collected during the exact period of exposure either by two bubblers fastened to the carrier or by two bubblers sampling from the chamber ports. Animals exposed to CG were kept under observation 10 days; those exposed to AC and CK, until death or complete recovery. Goats exposed to AC were weighed.

2. Determination of Respiratory Behavior.

To determine the respiratory behavior of the animal during exposure to the gas in question, the apparatus shown in Plates 1 and 4 was used. After equilibrium was established, the intake hose of the goat mask was connected to the chamber and the chamber atmosphere circulated through the mask at a rate of 30 to 34 liters per minute for the desired interval. This was done to eliminate the dead space of the mask. The slight negative pressure so produced did not appear to affect the respiratory behavior of the "masked" goat. At the termination of the exposure period the inlet hose was disconnected from the chamber and the mask flushed with clean air. Tracings showing pressure differences due to the goats' respiration were taken before, during, and after the exposure by means of the recording tambour. During the experiments with CG the inlet was connected to an MIXA2 canister before the exposure to protect the animal from any gas in the room. The resistance of the canister was found to alter the respiratory pattern slightly and, since the canister was found unnecessary, its use was discontinued thereafter.

Samples of gas were withdrawn from the chamber in duplicate during the period of exposure. Samples were also withdrawn from the mask in four instances during the CK exposures in order to compare mask and chamber concentrations. The results are presented in Table IX, and show that the concentrations were essentially the same.

3. Analytical Methods.

Samples of the chamber atmosphere were collected at a flow rate of one liter per minute regulated by critical pressure orifices. Flow rates were checked frequently with a calibrated wet test meter. The absorbing solutions used were 4% hexamethylenetetramine for CG, 4% sodium hydroxide in 30% ethanol for CK(2 bubblers), and 4% sodium hydroxide* for AC. Titrations for CG and CK content of the absorbing solution were made according to the mercuric nitrate method for chlorides in acid solution using diphenylcarbazone as indicator. Several drops of carbon tetrachloride were added to assist in seeing the end-point (Moody P.R. 2423 (1942)). AC was determined by the silver nitrate titration method of Liebig (Ann. Chem. und Pharm., 77, 102 (1851)), using potassium iodide as indicator.

* 8% NaOH was used at concentrations of 13 mg./liter and greater.

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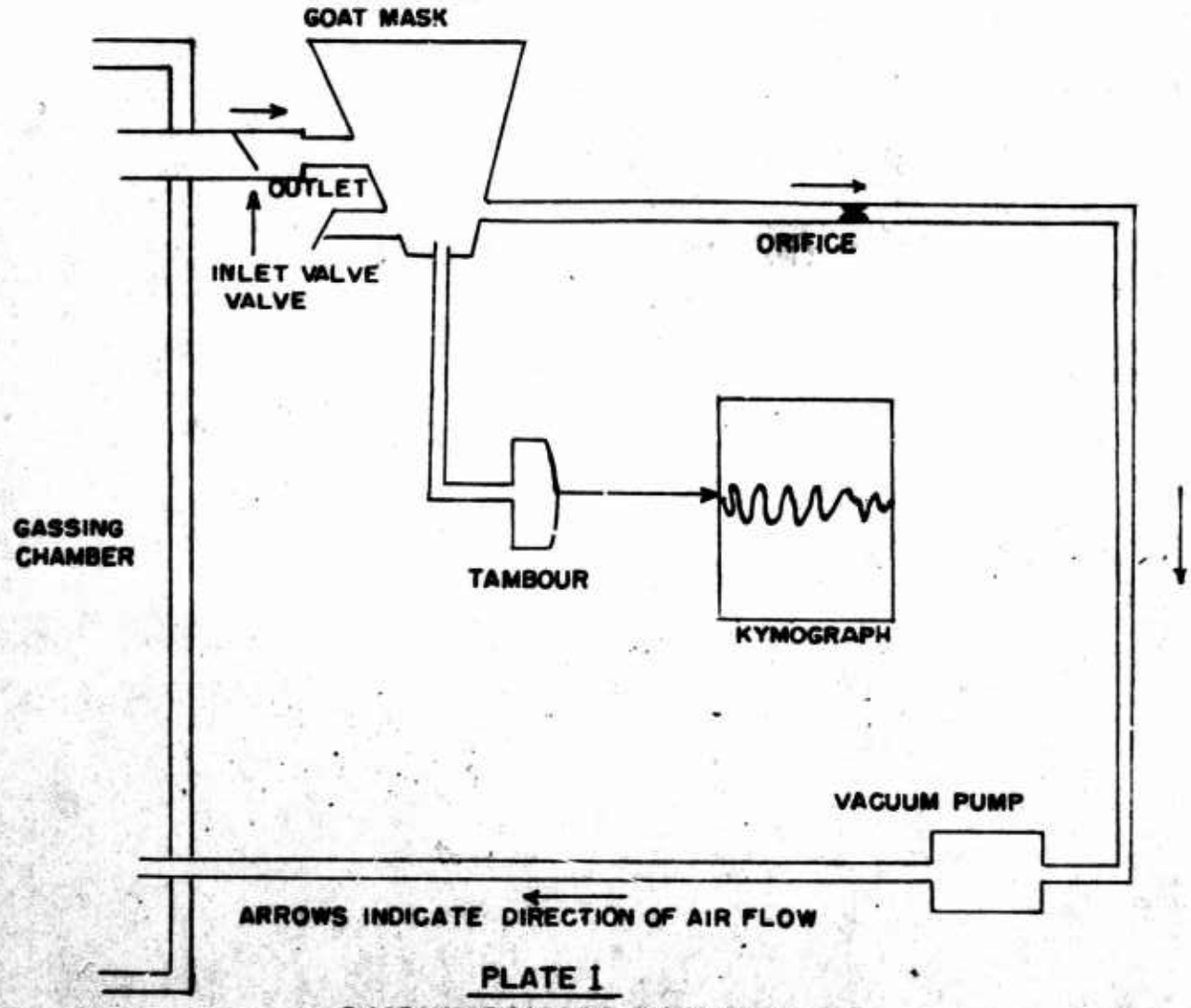

PLATE 1

DIAGRAM OF GASSING APPARATUS

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LEGEND

PLATE 3

Dynamic Flow Gassing Chamber.

A. Roller equipped carrier for introducing animals.

B. Atomizer in ice bath.

C. Manometer for measuring nitrogen flow.

D. Vigreaux type bubbler sampling from post.

E. Bubbler sampling on carrier.

F. Filter to protect orifice.

PLATE 4

Apparatus Used to Study Respiratory Behavior of Goats.

A. Goat mask.

B. Tambour.

C. Recorder for tambour.

D. Tube to vacumn pump.

E. Tube to tambour.

F. Outlet valve.

G. Intake hose leading to chamber post.

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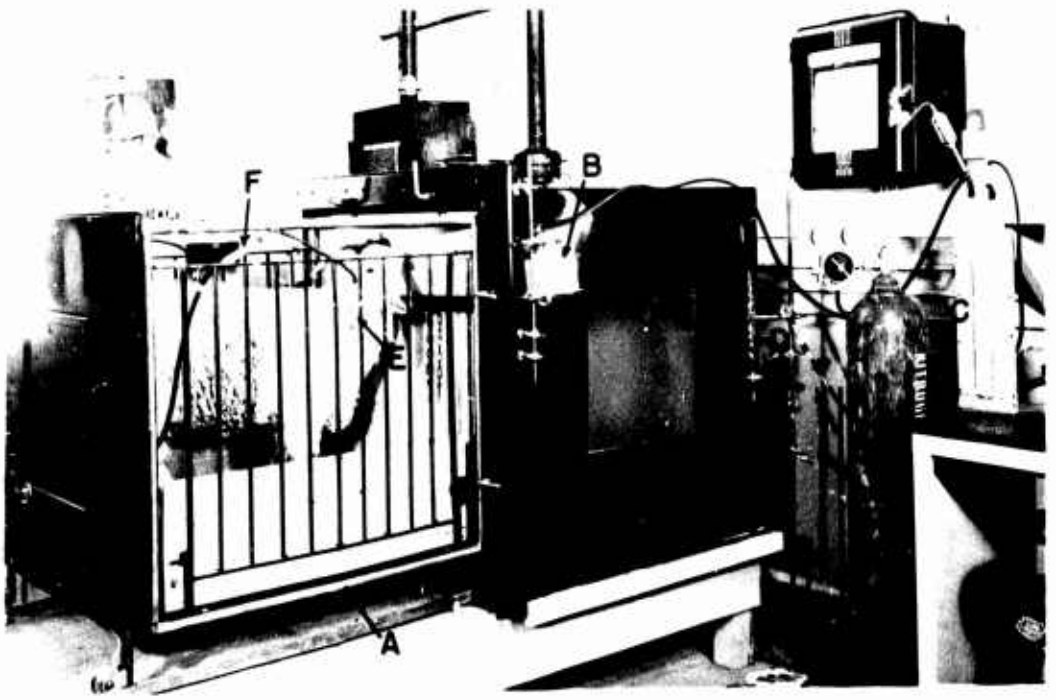

Plate 3. Dynamic Flow Gassing Chamber

Plate 4. Appratus used to study Respiratory Behavior of Goats.

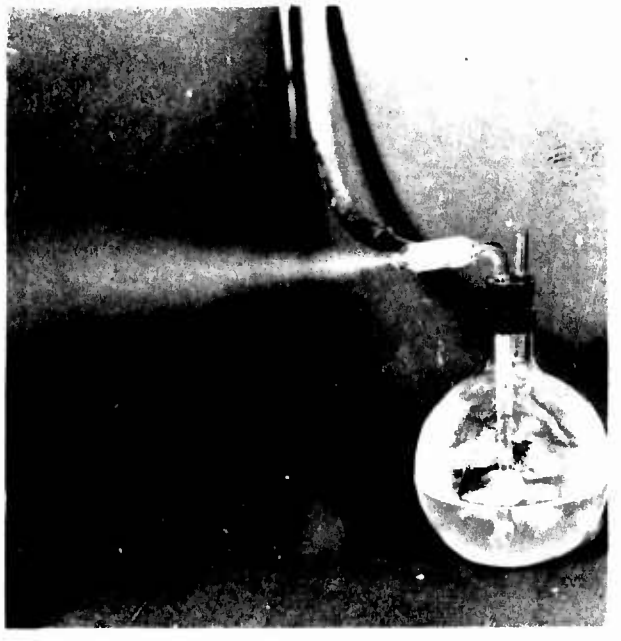

Plate 2. Atomizer for Dispersing CG, CK, and AC.

Photo No. 1585

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4. Operation of the Chamber.

The chamber flow rates and ratios of analytical to nominal concentrations for each series of runs are given in Table II. Analytical values are used in preference to nominal concentrations throughout this report for the following reasons: 1) The atomizers used for dispersing the agents tended to deliver more rapidly at the start of the run. 2) Evaporation losses occurred in weighing the agent. 3) Analytical samples were taken at a constant rate during the exact period of exposure and were thus not subject to errors caused by fluctuations in concentration.

TABLE II

Agent	Study	Time of Sample minute	Chamber Flow l./minute	Average Ratio of Analytical to Nominal Concentration
CG	L(Ct)50	2	1,050	0.75
CG	L(Ct)50	0.5	1,050	0.79
CG	Respiratory	0.5, 2	1,000	0.66
CK	L(Ct)50	2	1,000	0.73
CK	Respiratory	0.5, 2	1000, 750, 1650	0.65
AC	Respiratory	0.5, 2	1000, 750, 500	0.76
AC	L(Ct)50	0.5	2,900	0.79

A further check on the accuracy of sampling in the chamber was made comparing results obtained from collection bubblers mounted on the carrier and bubblers sampling through ports of the chamber. The carrier with the bubblers operating and with 3 goats was introduced into a chamber concentration of AC for a 30 second period. Port samples were taken for the same interval. The results of 20 such experiments yielded an average ratio of carrier to port concentrations of 0.99 with a standard error (σ) of 0.09. It is thus evident that the homogeneity of the chamber atmosphere was not appreciably disturbed by the introduction of animals, and that sampling on the carrier or from the ports was equally reliable.

D. Results.

1. L(Ct)50 Determinations

a. CG (t = 2 minutes, 30 seconds)

The L(Ct)50 for 2 minute total exposures of unmasked goats to CG is 6500 $\pm$ 750 mg.min./m^3, calculated by the method of Bliss (C.I. Bliss, Quart. J. Pharm., 11, 192 - 216 (1938)). The determination is based on the exposure of 72 goats. For 30 second exposures using 66 goats, the L(Ct)50 was indeterminate because mortality greater than 50% was attained only at Ct's between 10,000 and 12,000 mg.min./m^3. At greater Ct's the mortality probit curve exhibited a reverse trend. Detailed results are given in Tables III and IV, where the data are grouped for convenience in plotting. The Log Ct-probability curves are shown in Figures 1 and 2.

[redacted]

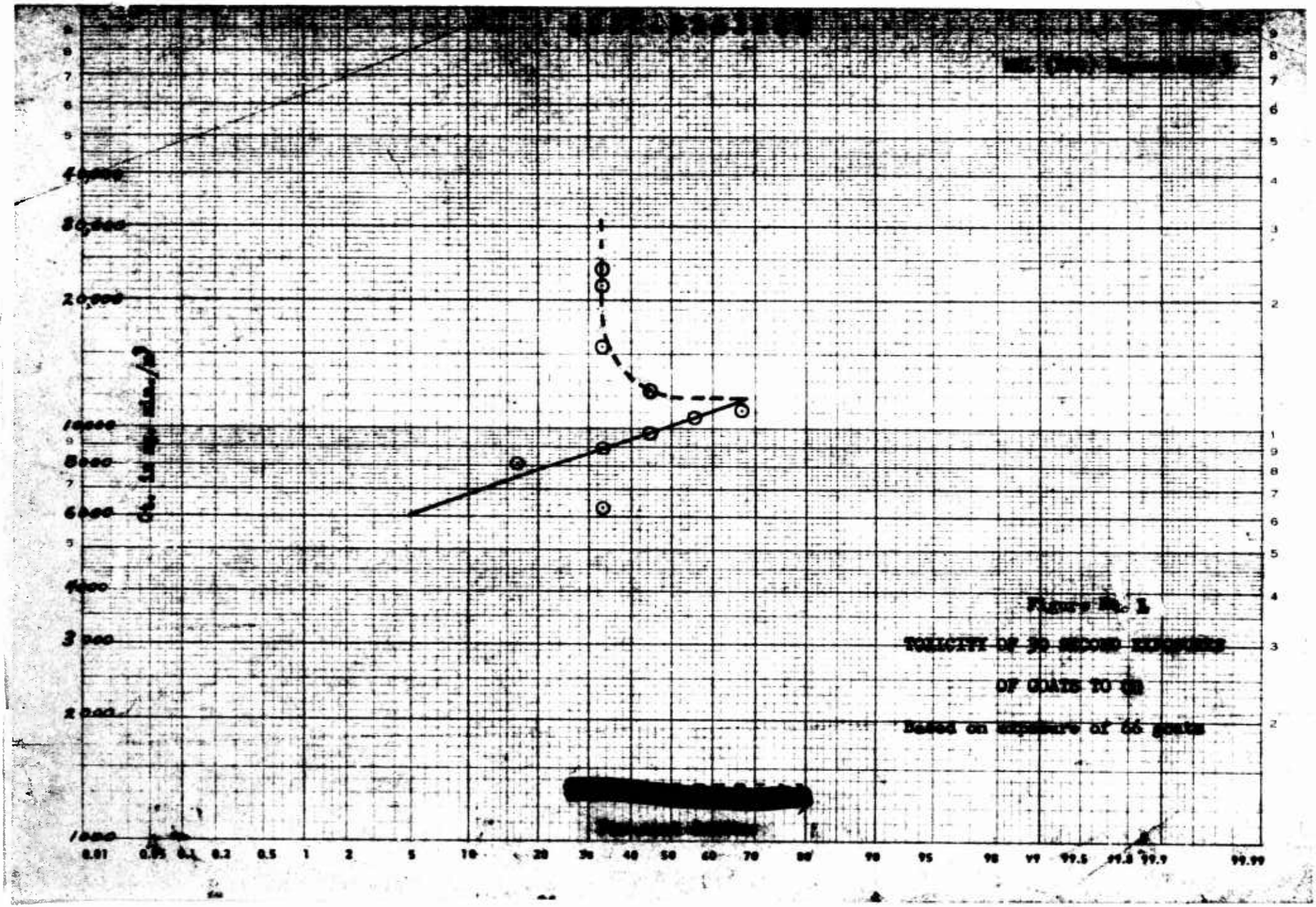


Figure No. 1

TOXICITY OF 30 SECOND EXPOSURE

OF GOATS TO [redacted]

Based on exposure of 66 goats

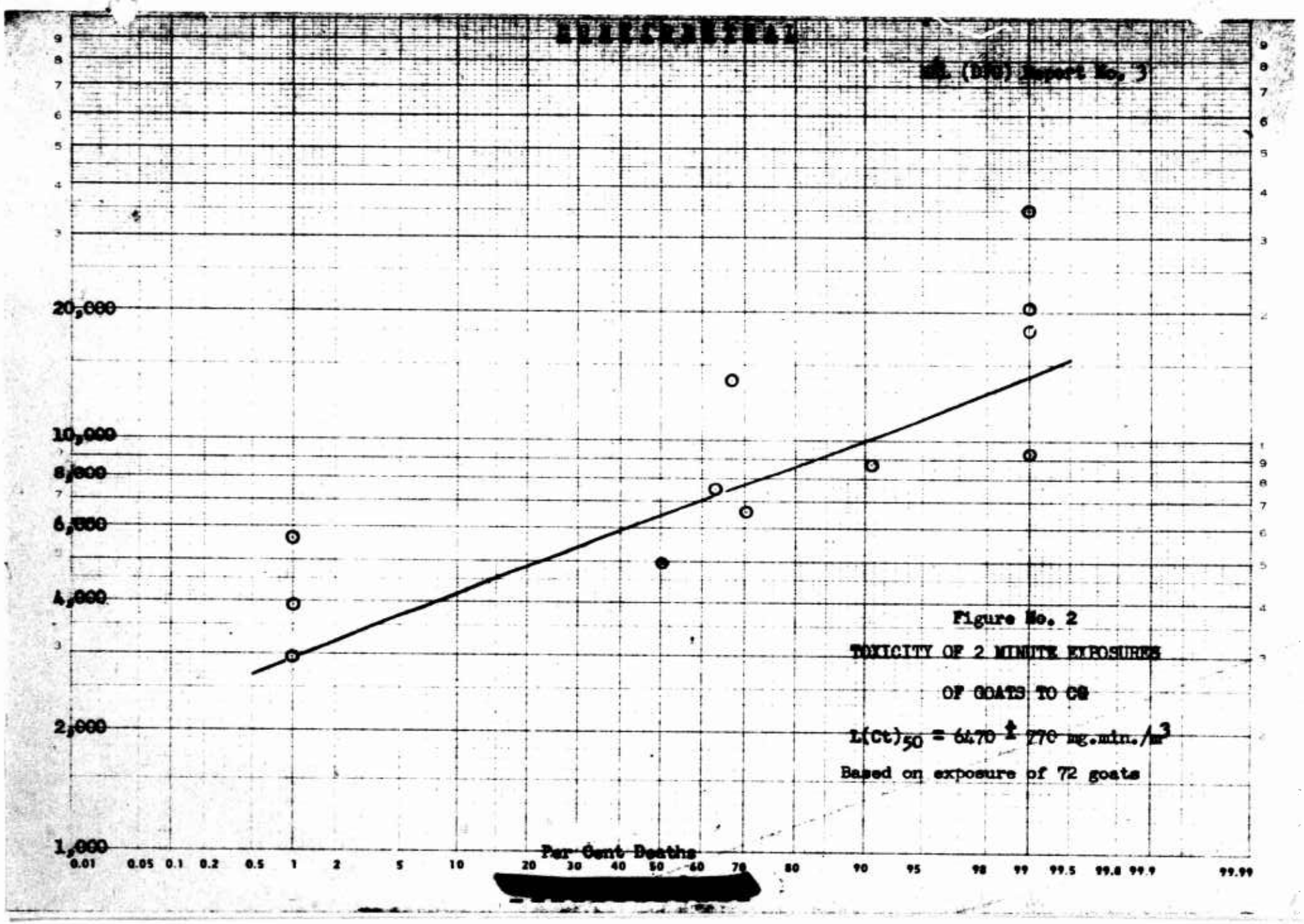


Figure No. 2

TOXICITY OF 2 MINUTE EXPOSURES

OF GOATS TO CG

$L(Ct)_{50} = 6470 \pm 270$ mg.min./m^3

Based on exposure of 72 goats

[redacted]

TABLE III

TOXICITY OF 30
SECOND EXPOSURES OF GOATS TO PHOSGENE

Run No.	Analytical Concentration mg./l.		Ct mg.min./m^3	Mortality	Deaths %
24	47.50		23,750	1/3	33.3
25	43.28		21,640	1/3	33.3
17	31.28		15,640	1/3	33.3
13	26.22		13,110	2/3	
18	23.70		11,850	1/3	
14	23.60		11,800	1/3	
		Av.	12,250	4/9	44.4
11	22.73		11,370	3/3	
19	22.26		11,130	2/3	
2	21.74		10,870	1/3	
		Av.	11,120	6/9	66.6
9	21.64		10,820	2/3	
10	21.32		10,660	1/3	
6	21.16		10,580	2/3	
		Av.	10,690	5/9	55.5
8	20.06		10,030	2/3	
16	19.70		9,850	1/3	
12	18.83		9,420	1/3	
		Av.	9,770	4/9	44.4
3	18.36		9,180	1/3	
15	18.10		9,050	1/3	
5	17.44		8,720	1/3	
		Av.	8,980	3/9	33.3
22	16.36		8,180	0/3	
1	16.04		8,020	1/3	
		Av.	8,100	1/6	16.6
4	13.80		6,900	1/3	
20	11.52		5,760	1/3	
		Av.	6,330	2/6	33.3

[redacted]

[redacted]

TABLE IV

TOXICITY OF TWO MINUTE EXPOSURES OF GOATS TO CG

Run No.	Analytical Concentration mg./l.	Ct mg.min./m^3	Mortality	Deaths %
30	17.50	35,000	3/3	100
29	10.23	20,460	3/3	100
27	8.98	17,960	2/2	100
28	6.98	13,960	2/3	67
14	4.63	9,260	3/3	100
18	4.41	8,820	3/3	
15	4.39	8,780	3/3	
16	4.31	8,620	2/3	
19	4.20	8,400	3/3	
		Av. 8,645	11/12	92
20	3.93	7,860	2/3	
6	3.90	7,800	2/2	
5	3.69	7,380	1/2	
4	3.61	7,220	1/2	
21	3.55	7,100	1/2	
		Av. 7,500	7/11	64
24	3.44	6,880	2/3	
26	3.36	6,720	2/3	
7	3.32	6,640	2/2	
12	3.27	6,540	2/2	
23	3.24	6,480	2/3	
3	3.21	6,420	1/2	
17	3.07	6,140	1/2	
		Av. 6,570	12/17	71
13	2.96	5,920	0/3	
11	2.83	5,630	0/2	
25	2.68	5,360	0/3	
		Av. 5,590	0/8	0
8	2.46	4,920	1/2	50
9	1.97	3,940	0/2	
2	1.91	3,820	0/2	
		Av. 3,880	0/4	0
10	1.49	2,980	0/2	
1	1.46	2,920	0/2	
		Av. 2,950	0/4	0

[redacted]

[redacted]

b. CK (t = 2 minutes)

The L(Ct)50 for 2 minute total exposures of unmasked goats to CK is 7000 ± 750 mg.min./m^3, calculated by the method of Bliss. Fifty-nine goats were used. Detailed results are shown in Table V and Figure 3.

c. AC (t = 30 seconds)

The L(Ct)50 for 30 second total exposure of unmasked goats to AC is 1300 mg.min./m^3 (48 animals). Grouping of the data for plotting is shown in Table VI and the log Ct-probability curve used to determine the L(Ct)50 is given in Figure 4. As no correlation was found between weight of the animal and toxicity, weights are not given.

2. General Response of Goats.

a. CG.

Goats exposed to casualty producing concentrations of CG exhibited no early symptoms except struggling during exposure. Difficulty in expiration immediately following exposure was severe enough in some instances to cause retraction of the intercostal spaces. About four hours after gassing, difficulty in respiration had increased and there was audible and visible evidence of pulmonary edema. Cyanosis followed and all symptoms increased until the time of death.

b. CK and AC.

Animals exposed to CK and AC showed an essentially similar train of symptoms. The first noticeable effect was dilatation of the pupils, which was more marked after exposure to CK than to AC. Respiratory stimulation then occurred and after about 30 seconds the goat bleated and struggled violently. The abdomen usually became distended at this time. A few seconds after struggling started the goat collapsed (25 to 60 seconds from the start of exposure). Respiratory stimulation continued for about 30 seconds and was followed by respiratory paralysis. While the animal was comatose tetanic spasms occurred and then changed to clonic convulsions. The convulsions continued at intervals until death or start of recovery of the animal. The goats that died usually struggled briefly just before death. In some instances (with both CK and AC), pulmonary and nasal hemorrhage were noted. Deaths usually occurred within 10 minutes of exposure.

Those animals which recovered resumed normal respiration slowly. Return of consciousness was gradual, and animals frequently relapsed after making too great an effort to rise. Upon recovery, the forelegs were weak, but in a short time the goat was alert and apparently unaffected. There were no residual symptoms or delayed deaths due to AC. Three of the goats totally exposed to CK exhibited severe residual neurological signs.

Cyanosis was present in both AC and CK gassed animals but was more pronounced with CK. Animals totally exposed to CK also exhibited marked lacrimation.

[redacted]

[redacted]

TABLE V

TOXICITY OF TWO MINUTE EXPOSURES OF GOATS TO CK

Run No.	Analytical Concentration mg./l.	Ct mg.min./m^3	Mortality	Deaths %
21	8.10	16,200	3/3	100
22	5.89	11,780	3/3	100
1	5.38	10,760	3/3	100
2	4.90	9,800	3/3	
18	4.88	9,760	2/3	
11	4.70	9,400	3/3	
		Av. 9,650	8/9	89
16	4.34	8,680	2/3	
10	4.05	8,100	1/3	
		Av. 8,390	3/6	50
15	3.90	7,800	3/3	
20	3.60	7,200	3/3	
6	3.54	7,080	2/3(1)	
9	3.50	7,000	2/3	
		Av. 7,520	10/12	83
8	3.42	6,840	0/3(1)	
7	3.20	6,400	1/3	
		Av. 6,620	1/6	17
3	2.92	5,840	1/3	
5	2.81	5,620	0/3	
		Av. 5,730	1/6	17
12	2.33	4,660	0/3(2)	
13	2.17	4,340	0/3	
14	2.16	4,320	1/3	
		Av. 4,440	1/9	11
19	1.94	3,880	0/3	0
17	1.41	2,820	0/3	
4	1.11	2,240	0/3	
		Av. 2,530	0/6	0

Notes: (1) One goat suffered severe neurological symptoms for three days after exposure. It was then sacrificed but counted as a survivor in the calculation of the L(Ct)50.
(2) One goat showed severe after effects for three days but slowly recovered.

[redacted]

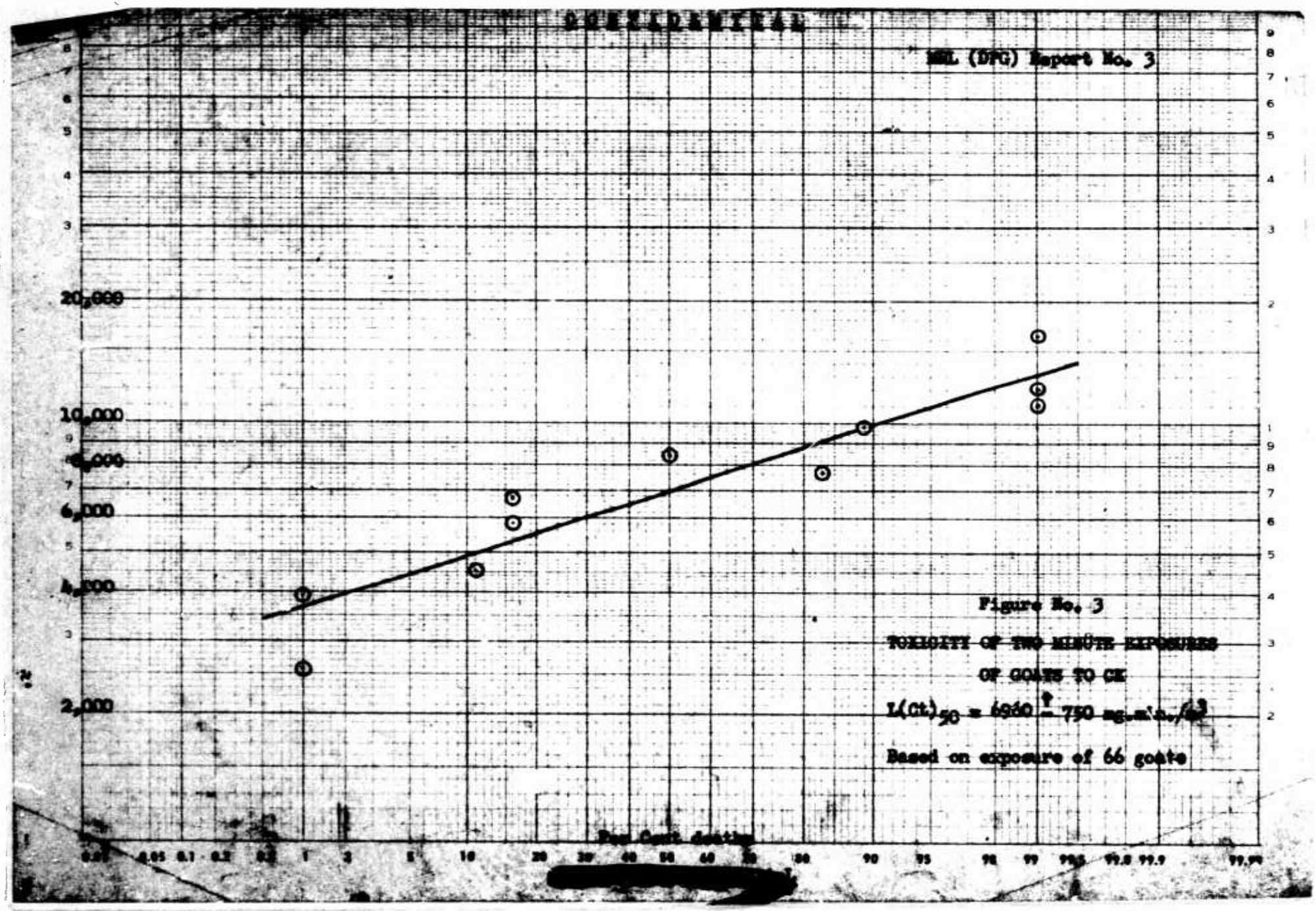


Figure No. 3

TOXICITY OF TWO MINUTE EXPOSURES OF GOATS TO CE

$L(Ct)_{50}$ = 6960 ± 750 mg.m.in./m³

Based on exposure of 66 goats

[redacted]

TABLE VI

TOXICITY OF 30 SECOND EXPOSURES OF GOATS TO AC

Run No.	Analytical Concentration mg./l.		Ct. mg.min./m^3	Time from Start of Exposure for Death Min.	Mortality	Deaths %
1	6.22		3,110	7, 8, 4	3/3	100
2	5.38		2,690	8, 7, 4	3/3	100
13	5.10		2,550	7	1/1	100
12	4.37		2,185	3	1/1	100
3	4.14		2,070	7, 8, 5	3/3	100
14	3.44		1,720	10, 10, 11	3/3	100
8	3.09		1,545	7, 6, 10	3/3	100
17	2.74		1,370	13	1/3	
20	2.72		1,360	--	0/1	
4	2.71		1,355	25, 7	2/3	
9	2.69		1,345	10	1/1	
10	2.64		1,320	7	1/1	
16	2.63		1,315	8, 12, 6	3/3	
		Av.	1,345		8/12	66.7
19	2.41		1,205	--	0/3	
15	2.39		1,195	--	0/3	
18	2.36		1,190	35	1/3	
7	2.27		1,135	--	0/3	
		Av.	1,180		1/12	8.4
11	2.24		1,120	--	0/1	0
5	2.12		1,060	--	0/3	0
6	1.99		995	--	0/3	0

[redacted]

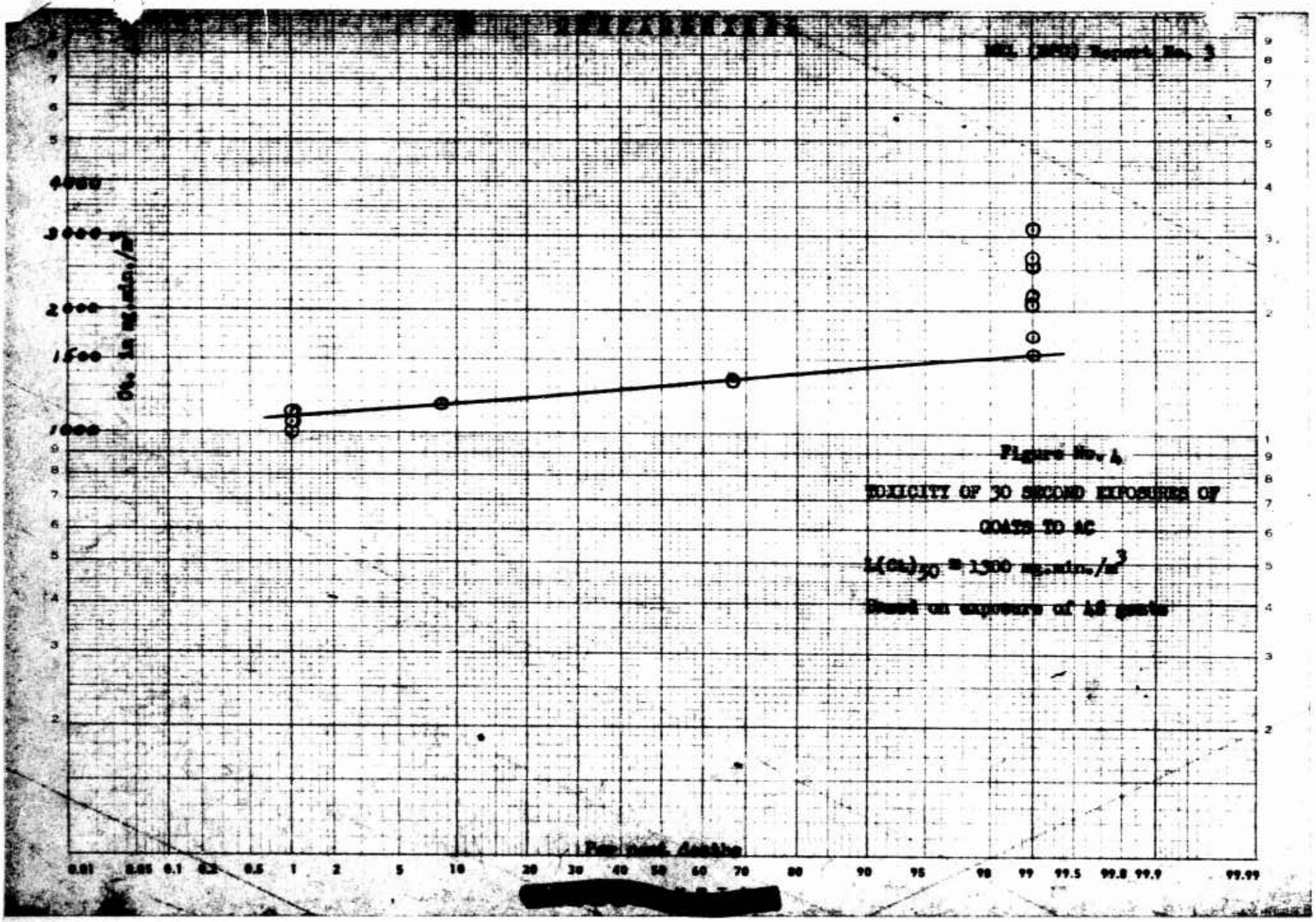


Figure No. 4

TOXICITY OF 30 SECOND EXPOSURES OF COAST TO AC

LC_{50} = 1300 mg.min./m^3

Based on exposure of 18 guests

[redacted]

3. Respiratory Behavior of "Masked" Goats.

a. CG.

Seven goats wearing the modified mask were exposed for 30 seconds to CG in concentrations of 25 to 50 mg./l. (Ct's of 12,500 to 25,000 mg.min./m^3). Six of these animals showed complete breath holding during the entire exposure, and exhibited no symptoms of CG poisoning. One goat exposed to 35.3 mg./l. took 18 shallow breaths and died as a result.

In another series of experiments 19 "masked" goats were exposed to concentrations of 0.6 to 15.7 mg./l. of CG for the duration of breath holding plus 30 seconds thereafter. Breath holding of 15 to 139 seconds was a constant response to concentrations above 1.3 mg./l. Below this concentration breath holding was not present in animals exposed for two minutes but respiration was depressed. At 0.37 mg./l. breathing was essentially normal. In one instance a goat was exposed to a concentration of 1.5 mg./l. for 12 minutes (Ct = 18,000 mg.min./m^3) without adverse effects, because of depression of the respiratory minute volume (Figure 7). Details of these results are shown in Table VII and representative tracings of the respiratory patterns are presented in Figures 5-8.

b. CK.

A total of 42 "masked" goats was exposed for 30 seconds or 2 minutes to concentrations of CK ranging from 0.54 to 51.6 mg./l. (Table VIII and IX). The general respiratory pattern for both exposure periods consisted of an initial period of respiratory depression with or without actual breath holding, followed by a period of respiratory stimulation and another period of depression. The initial depression (25 to 130 seconds) was observed in all exposures to concentrations of 2.0 mg./l. or higher. Eleven out of 42 goats exhibited breath holding. Below 2.0 mg./l. the initial respiratory phase was essentially normal. The depressed phase was followed by a stimulated phase characterized by deep, rapid, and regular breathing. The second depressed phase was characterized by slow, regular breathing of approximately normal depth. Representative tracings of these exposures are presented in Figures 9 to 15.

c. AC.

A total of 45 "masked" goats was exposed to AC for 2 minutes, 30 seconds or 15 seconds at concentrations of 0.8 to 45.0 mg./l. (Tables X and XI). With this gas, the immediate response to exposure differed from that to CG and CK in that respiratory depression occurred only in concentrations higher than 16.4 mg./l. In all other exposures respiration was normal for a brief initial period (5 to 60 seconds). This initial period of normal respiration was followed by progressive respiratory stimulation, usually occurring after the first 5 to 10 breaths. It was characterized by deep, rapid, and regular breathing. The stimulated phase was followed by marked respiratory depression.

[redacted]

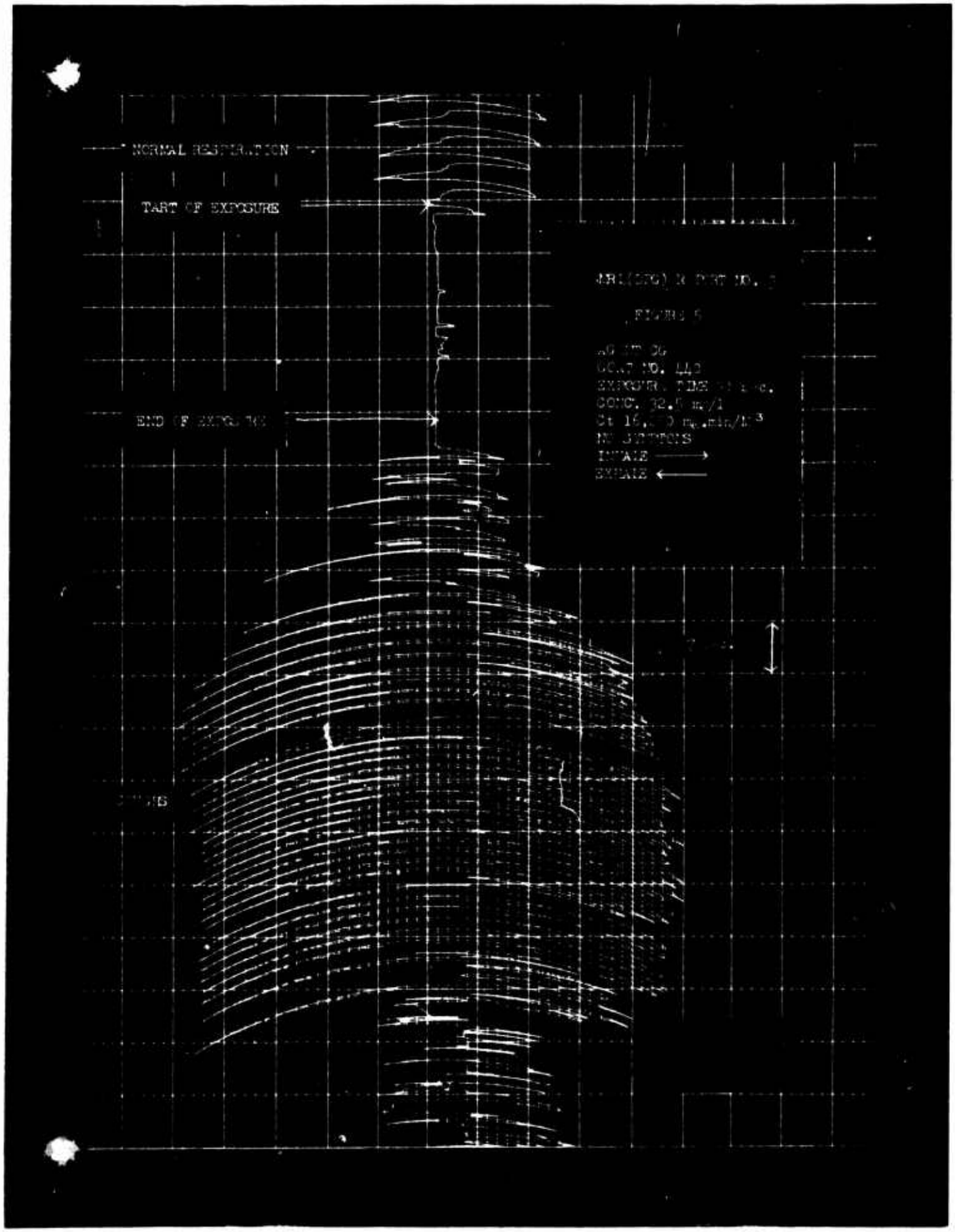
TABLE VII

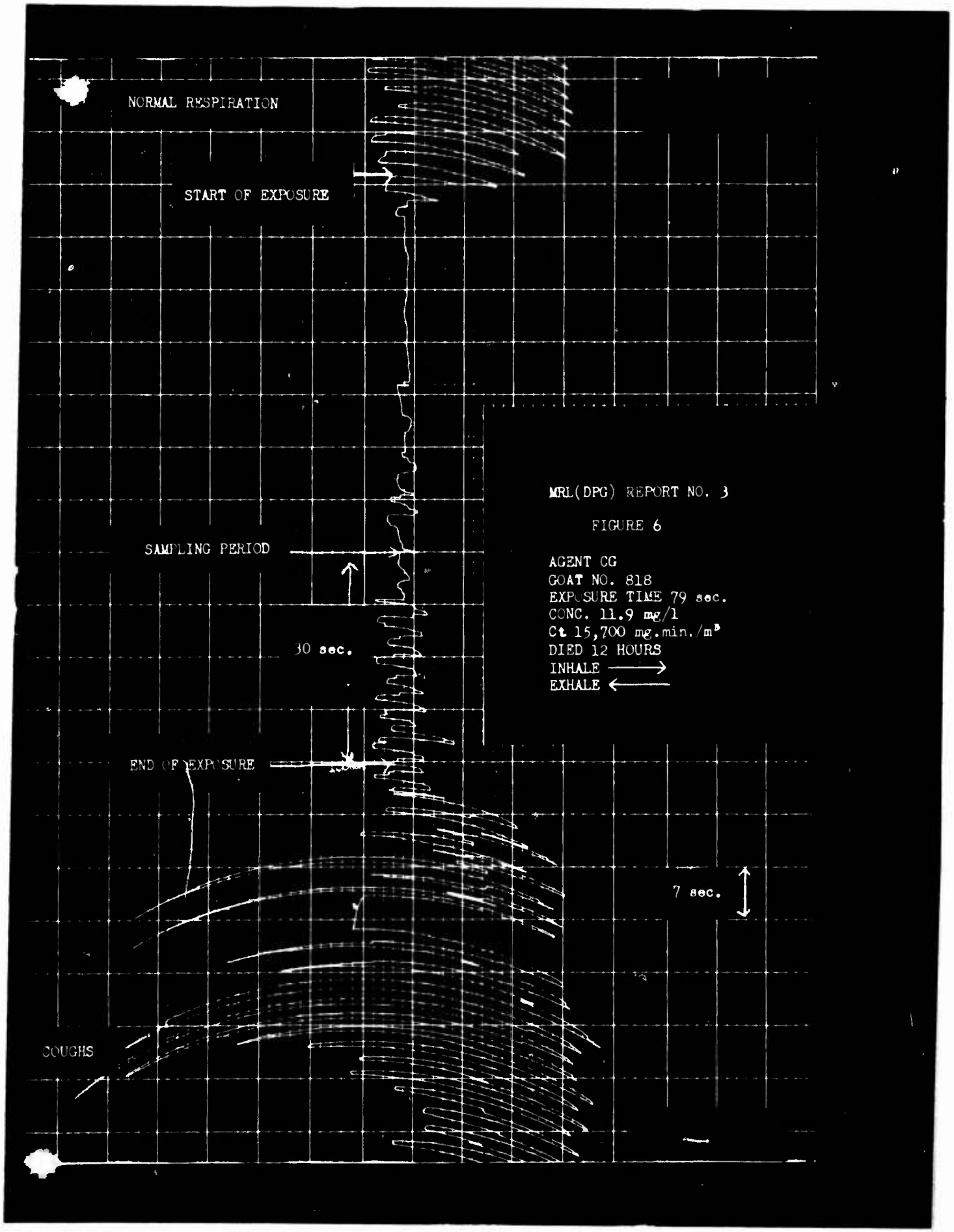
RESPIRATORY BEHAVIOR OF GOATS*EXPOSED TO CG

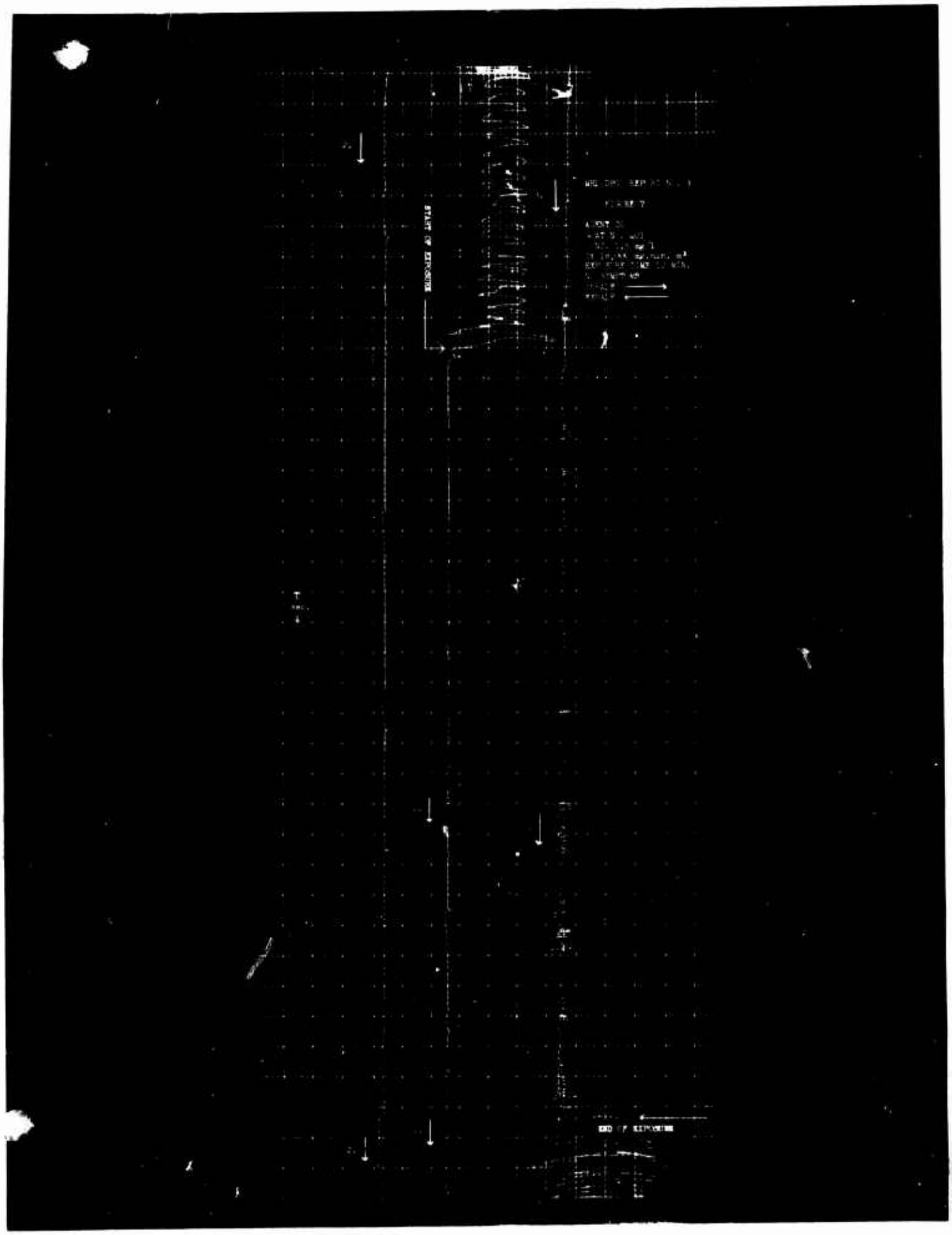
Goat Number	Analytical Concentration Mg./l.	Total Exposure Time Sec.	Analytical Ct mg.min./m^3	Respiratory Behavior: Time of Breath Holding Sec.	Respiratory Behavior: Character of Resumed Respiration During Exposure	Response of Goat to Agent	Figure Number
737	50.1	30	25,000	30	Complete breath holding	No symptoms	
1396	35.3	30	17,700	0	18 shallow breaths	Died - 26 hours	
862	34.5	30	17,300	30	Complete breath holding	No symptoms	
440	32.5	30	16,300	30	Complete breath holding	No symptoms	5
20	31.3	30	15,700	30	Complete breath holding	No symptoms	
242	26.8	30	13,400	30	Complete breath holding	No symptoms	
815	25.9	30	13,000	30	Complete breath holding	No symptoms	
144	15.7	65	17,000	35	11 shallow breaths	Died - 12 hours	
60	15.1	85	21,400	55	6 shallow breaths	No symptoms	
61	12.9	115	24,800	85	15 shallow breaths	Died - 12 hours	
818	11.9	79	15,700	49	11 shallow breaths	Died - 24 hours	6
183	8.9	102	15,300	72	5 shallow breaths	No symptoms	
354	8.5	82	11,600	52	6 shallow breaths	No symptoms	
UNG	8.5	157	22,200	127	11 shallow breaths	Died - 24 hours	
403	8.2	68	9,300	38	13 shallow breaths	Moderate casualty-recovered	
1301	4.2	102	7,100	72	8 shallow breaths	No symptoms	
25	3.6	169	10,100	139	4 shallow breaths	No symptoms	
541	2.4	76	3,000	46	12 mod. shallow breaths	Died - 24 hours	
401	1.5	720	18,000	60	Extremely shallow, slow	No symptoms	7
603	1.4	77	1,800	47	8 shallow breaths	No symptoms	
389	1.3	45	1,000	15	7 shallow breaths	No symptoms	
73	1.0	120	2,000	0	Mod. shallow, irregular	No symptoms	
382	0.98	120	1,960	0	Mod. shallow, irregular	No symptoms	8
762	0.85	120	1,690	0	Mod. shallow, slow, irreg.	No symptoms	
17	0.60	330	3,300	0	Shallow, slow, irregular	No symptoms	
711	0.37	120	740	0	Normal breathing	No symptoms	

* Wearing masks

All times are from start of exposure.


NORMAL RESPIRATION
TART OF EXPOSURE
END OF EXPOSURE
INTAKE
OUTAKE


NORMAL RESPIRATION
START OF EXPOSURE
SAMPLING PERIOD
30 sec.
END OF EXPOSURE
7 sec.
COUGHS
MRL(DPG) REPORT NO. 3
FIGURE 6
AGENT CG
GOAT NO. 818
EXPOSURE TIME 79 sec.
CONC. 11.9 mg/l
Ct 15,700 mg.min./m³
DIED 12 HOURS
INHALE
EXHALE



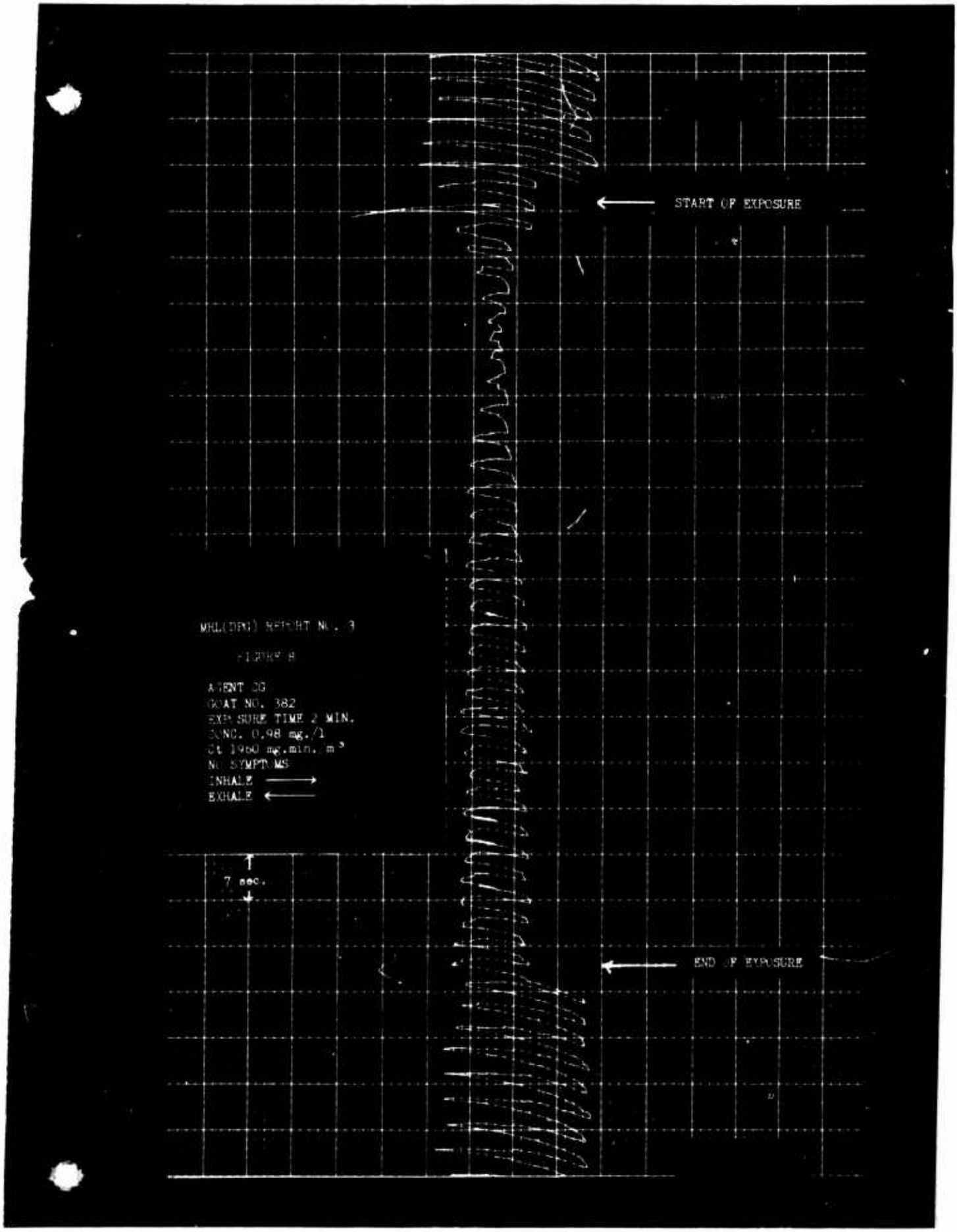

START OF EXPOSURE
MRL(DBG) RESEARCH NO. 3
AGENT CG
GOAT NO. 382
EXPOSURE TIME 2 MIN.
CONC. 0.98 mg./l
Ct 1960 mg.min. m³
NO SYMPTOMS
INHALE
EXHALE
7 sec.
END OF EXPOSURE

TABLE VIII

RESPIRATORY BEHAVIOR OF GOATS[1] EXPOSED TO CK FOR 30 SECONDS

Goat Number	Analytical Concentration Mg./l.	Analytical Ct mg.min./m^3	Character of Respiration During Exposure	Response Other Than Cyanosis	Recovery Time Min.	Figure Number
832	51.6	25,800	Moderate depth, rapid, irregular	Died	--	
160	46.0*	23,000	Breath holding-12 sec.extremely shallow-18 seconds	None	I	
99	39.2	19,600	Shallow, rapid, irregular	None	I	
53	35.4	17,700	Shallow, rapid, irregular	None	I	
106	35.0	17,500	Extremely shallow, rapid, irregular	None	I	
494	21.9	10,950	Extremely shallow, rapid, irregular	None	I	
804	21.6	10,800	Normal depth, rapid, irregular	Died	--	
723	21.4	10,700	Slow, irregular, 2 deep breaths	None	I	
1311	21.1	10,550	Breath holding-6 sec. shallow, slow, irreg.-24 sec.	None	I	
54	19.7	9,850	Shallow, irregular, rapid, 2 deep breaths	Convulsions	23	
853	19.6	9,800	Extremely shallow, irregular	None	I	15
352	19.2	9,600	Breath holding-6 sec.,shallow, rapid, irreg.-24 sec.	None	I	
170	18.2	9,100	Shallow, rapid, 22 sec., deep, rapid-8 sec.	Died	--	13
UNG	18.2	9,100	Normal depth, irregular, rapid	Convulsions	14	
428	17.3	8,650	Breath holding-17 sec., slow, 2 deep breaths-13 sec.	Convulsions	10	
107	16.8	8,400	Normal depth, rapid, irregular	Convulsions	20	
833	15.6	7,800	Breath holding-10 sec., rapid 3 deep breaths-20 sec.	Convulsions	10	14
91	13.2	6,600	Breath holding-20 sec., shallow, rapid-10 sec.	None	I	

1 Wearing masks
* Analytical Sample Lost. Concentration calculated from an A/N ratio of 0.60
I Immediate recovery

All times are from start of exposure.
Deaths occurred within 5 minutes after start of exposure.

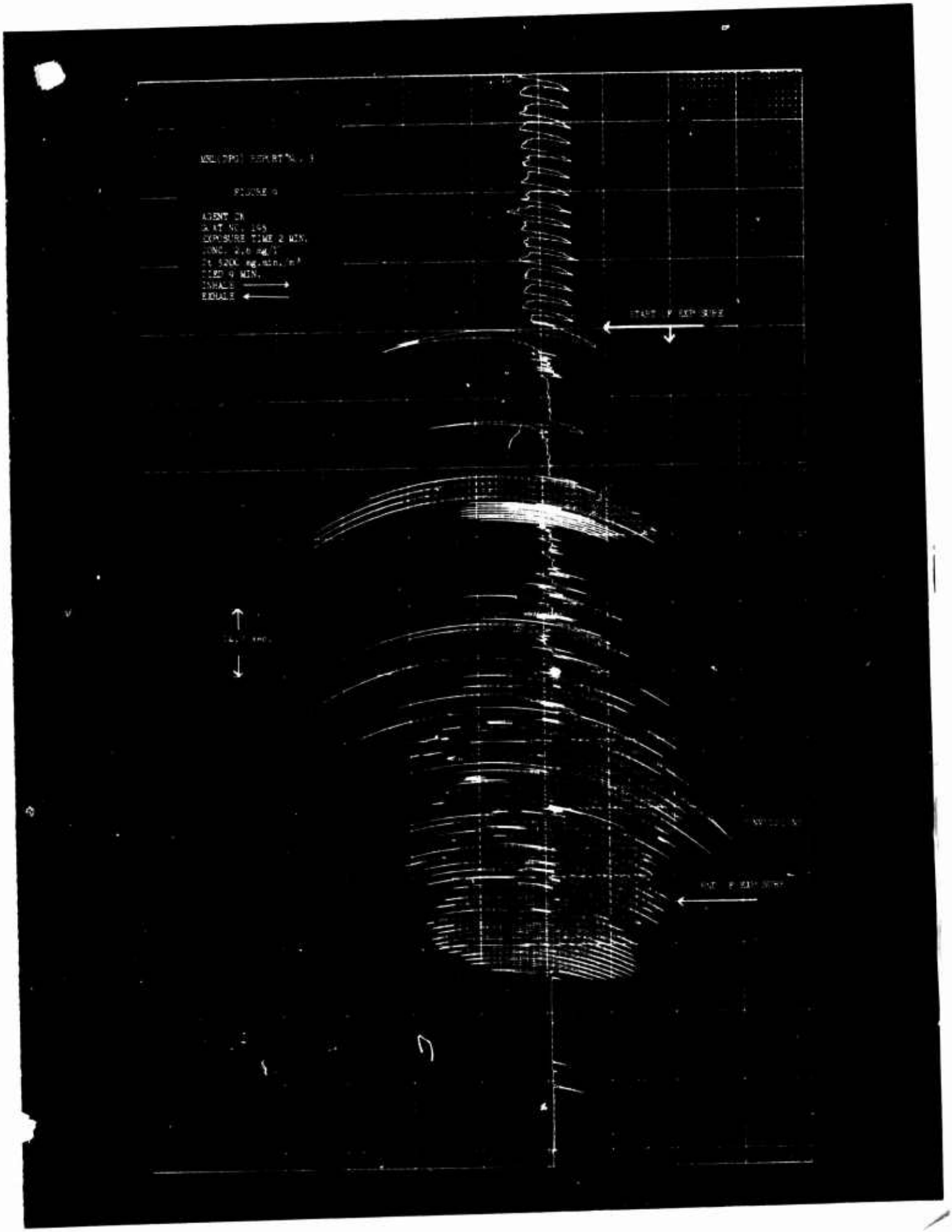
TABLE I

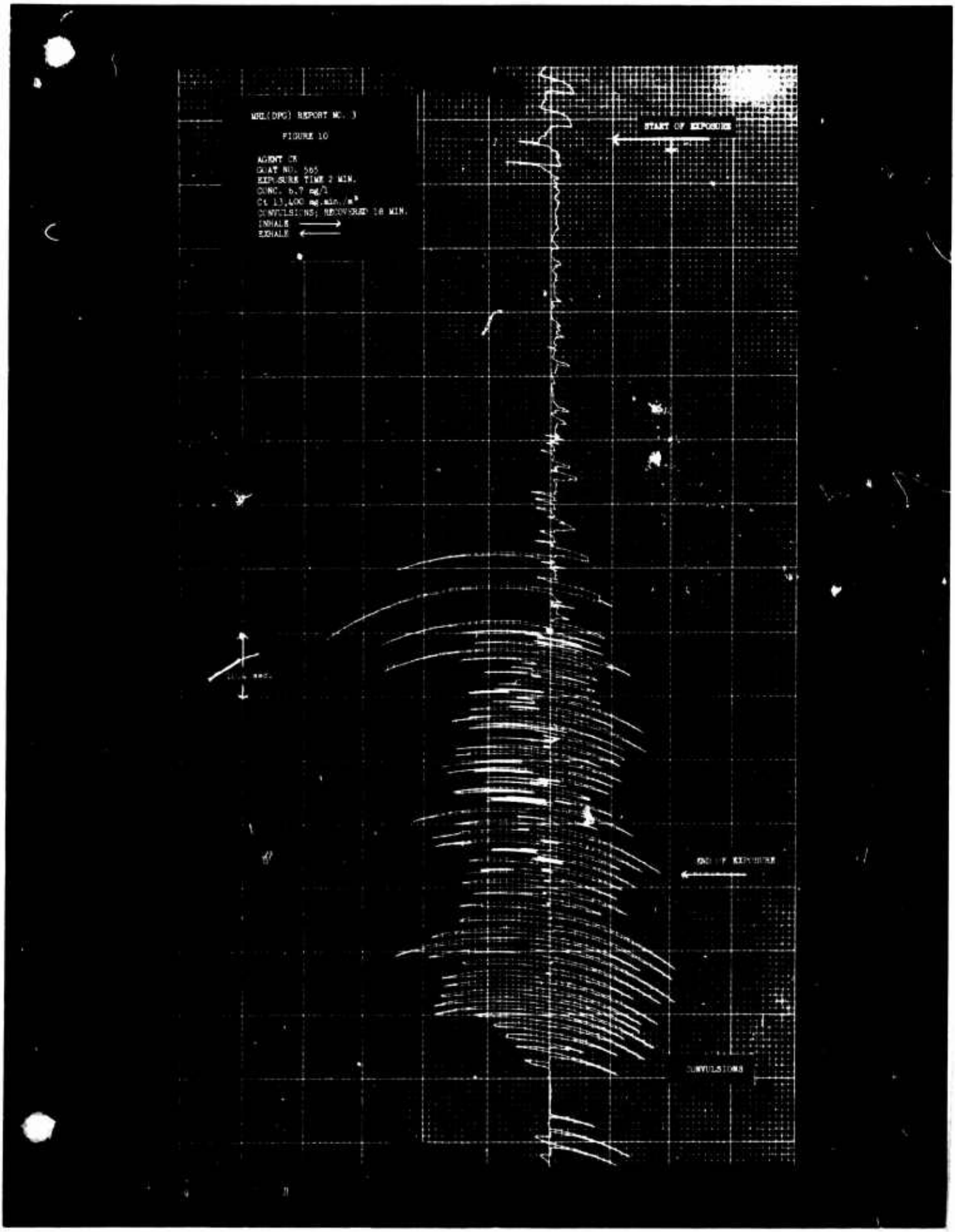
RESPIRATORY BEHAVIOR OF GOATS EXPOSED TO CK FOR 2 MINUTES

Goat No.	Analytical Concentration: Chamber mg./l.	Analytical Concentration: Mask mg./l.	Chamber-Mask Conc. Ratio	Analytical Ct (Chamber) mg.min./m³	Character of Respiration During Exposure: Depressed Phase	Depressed Phase Duration Sec.	Stimulated Phase Duration Sec.	Response Other than Cyanosis	Recovery Time Min.	Figure No.
829	12.5			25,000	Shallow, slow, irregular	60	60	Died	--	
437	8.51			17,020	Extremely shallow, irregular	60	60	Died	--	
838	8.10			16,200	Breath holding-40 sec., shallow irregular-35 sec.	75	45	Died	--	
1337	8.00	7.76	0.97	16,000	Mod. shallow, irregular	130*	After Exposure	None	I	11
196	6.89			13,780	Extremely shallow, irregular	30	90	Convulsions	25	
737	6.83			13,600	Shallow, irregular	60	60	Convulsions	10	
565	6.75			13,500	Breath holding-60 sec. shallow-20 sec.	80	40	Convulsions	20	10
618	6.65			13,300	Shallow, irregular	30	90	Convulsions	18	
520	6.24	6.00	0.96	12,480	Breath holding-20sec.irreg.40sec.	60	60	Convulsions	90	
112	6.03	5.37	0.89	12,060	Shallow, slow	25	155	Convulsions	50	
326	5.30			10,600	Shallow, irregular	60	60	Died	--	
577	4.41			8,820	Breath holding	70	50	Weakness	5	
351	4.25			8,500	Shallow, slow	60	60	None	I	
195	2.59			5,180	Breath holding	25	95	Died	--	9
29	2.54			5,080	Shallow, irregular	30	90	None	I	
53	2.41			4,820	Shallow, irregular	60	60	None	I	
650	1.98			3,960	Normal Respiration	30**	90	None	I	
411	1.90			3,800	Normal Respiration	60**	60	Weakness	5	
175	1.82			3,640	Normal Respiration	35**	85	Convulsions	9	
69	1.72			3,440	Normal Respiration	75**	45	None	I	12
32	1.55	1.46	0.94	3,100	Slow, irregular	85	35	None	I	
486	1.31			2,620	Normal Respiration			None	I	
561	1.18			2,360	Normal Respiration			None	I	
113	0.54			1,080	Normal Respiration			None	I	

* Depressed phase lasted until after exposure ended.
** Intervals of normal respiration before onset of stimulated phase.
All deaths were within 24 hrs. of start of exposure.

I - Immediate Recovery
All times are from start of exposure


AGENT CN
INHALE
EXHALE


WRL(DPG) REPORT NO. 3
FIGURE 10
AGENT CR
GUAT NO. 565
EXPOSURE TIME 2 MIN.
CONC. 6.7 mg/l
Ct 13,400 mg.min./m³
CONVULSIONS; RECOVERED 18 MIN.
INHALE
EXHALE
START OF EXPOSURE
CONVULSIONS

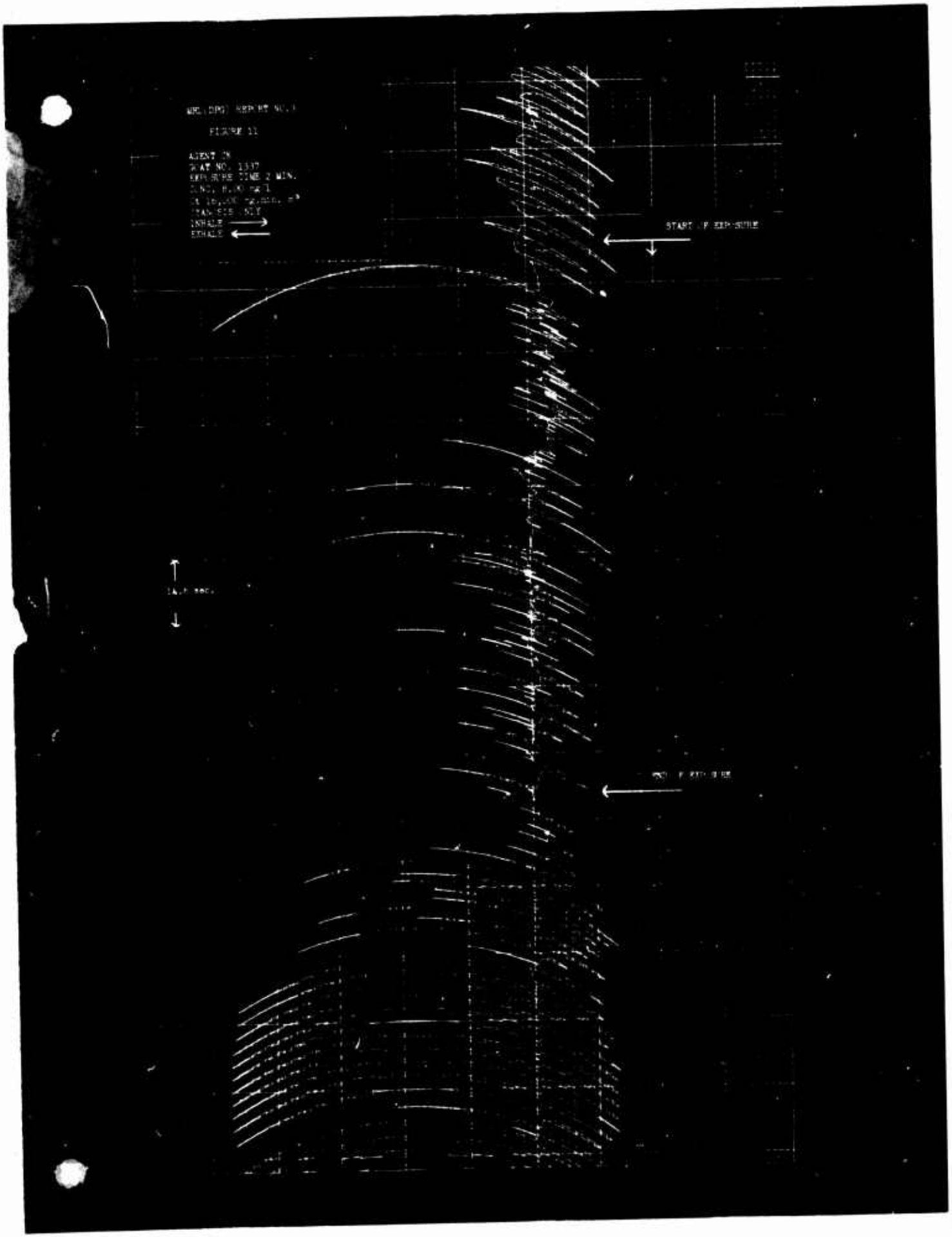
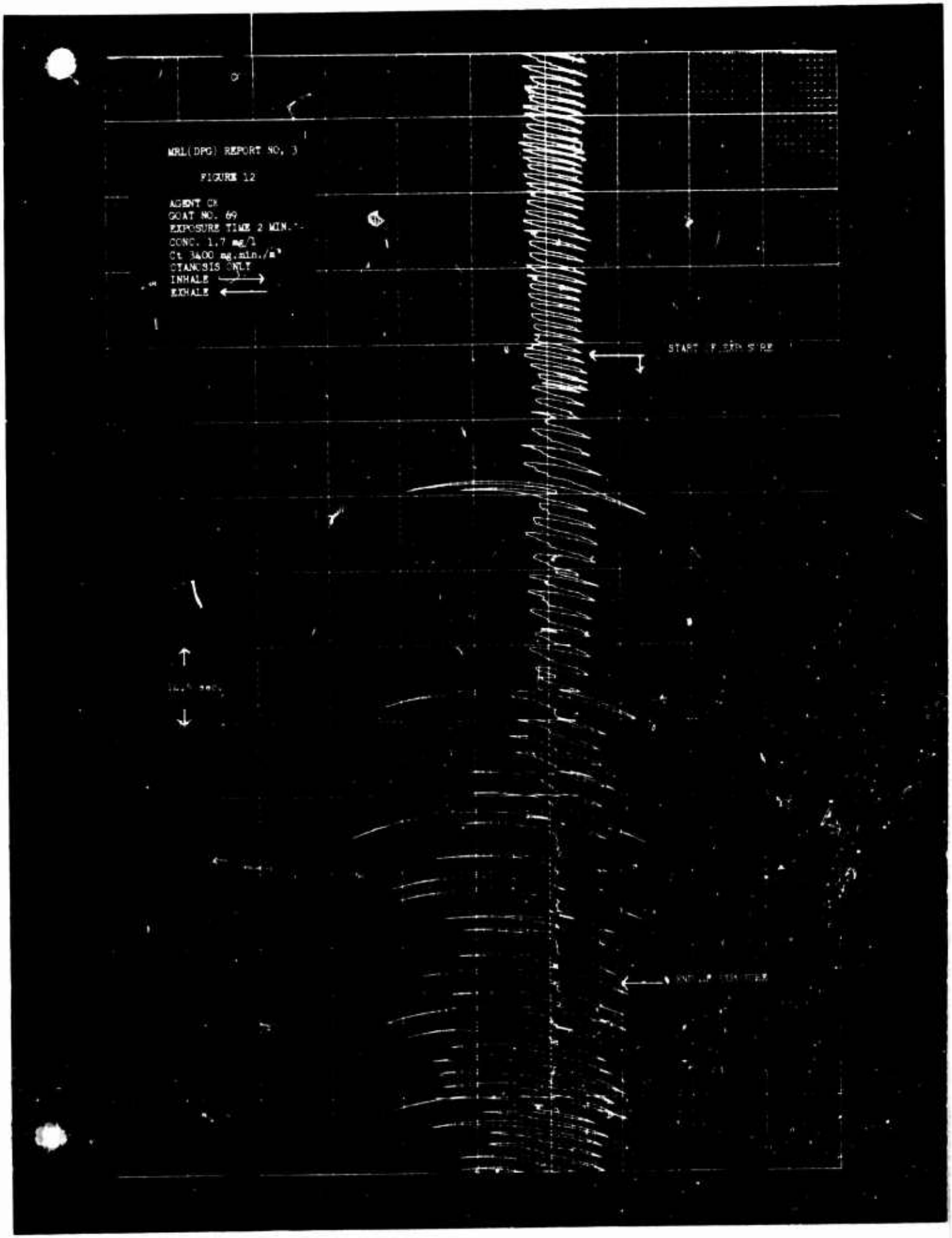
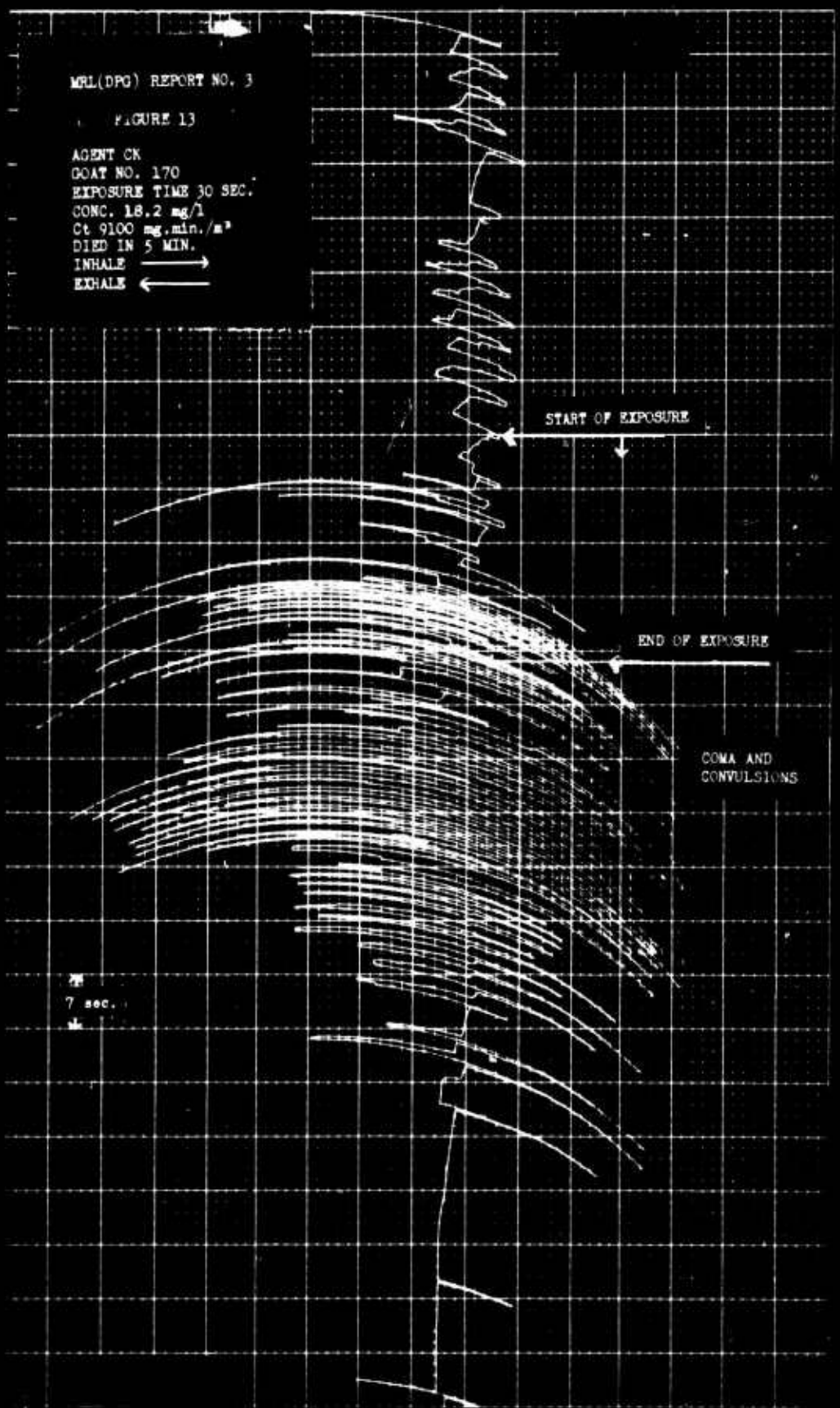
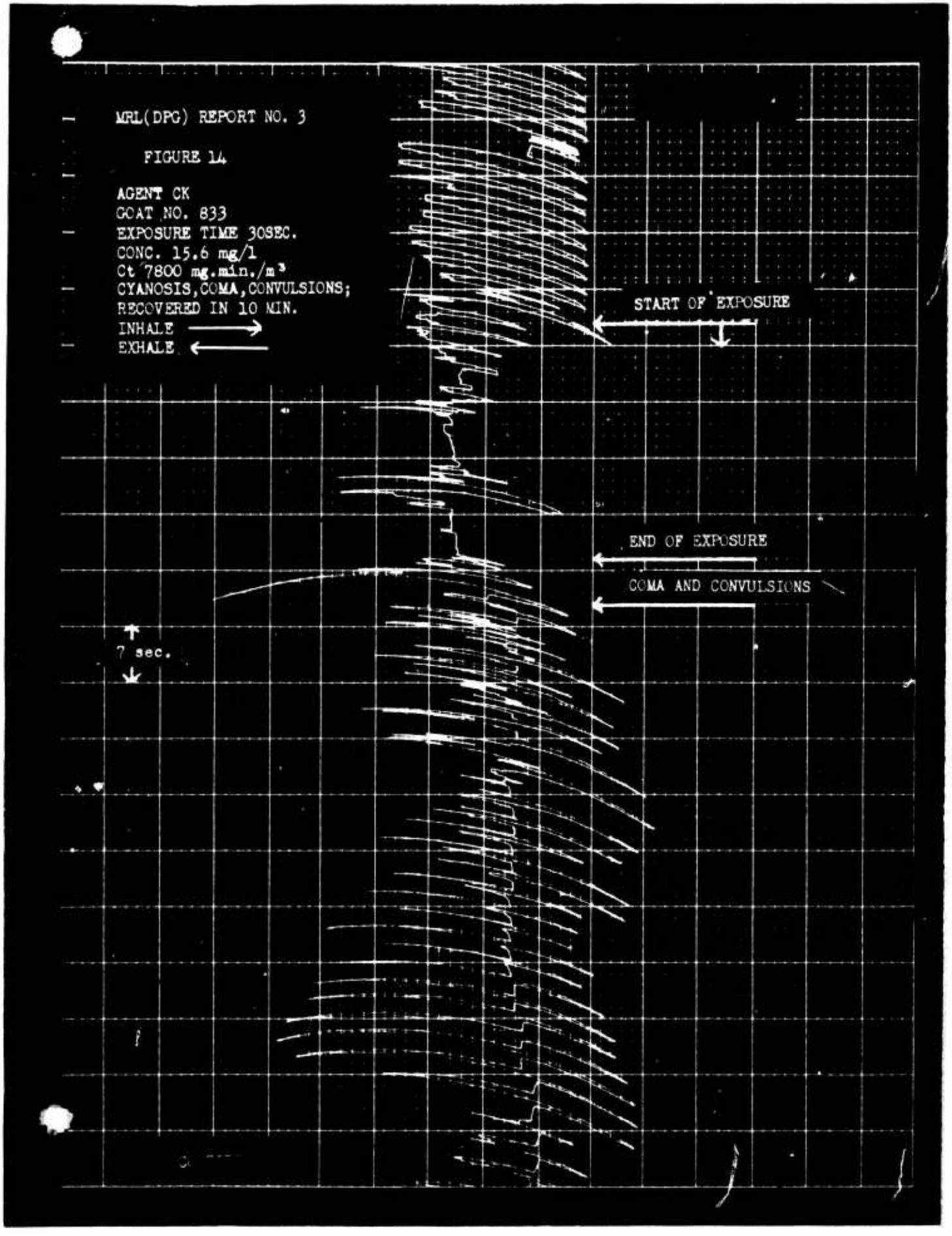


FIGURE 11
AGENT CN
RAT NO. 1337
EXPOSURE TIME 2 MIN.
INHALE
EXHALE
START OF EXPOSURE


WRL(DPG) REPORT NO. 3
FIGURE 12
AGENT CX
GOAT NO. 69
EXPOSURE TIME 2 MIN.
CONC. 1.7 mg/l
Ct 3400 mg.min./m³
CTANOSIS ONLY
INHALE
EXHALE


MRL(DPG) REPORT NO. 3
FIGURE 13
AGENT CK
GOAT NO. 170
EXPOSURE TIME 30 SEC.
CONC. 18.2 mg/l
Ct 9100 mg.min./m³
DIED IN 5 MIN.
INHALE
EXHALE
START OF EXPOSURE
END OF EXPOSURE
COMA AND CONVULSIONS
7 sec.


MRL(DPG) REPORT NO. 3
FIGURE 14
AGENT CK
GOAT NO. 833
EXPOSURE TIME 30SEC.
CONC. 15.6 mg/l
Ct 7800 mg.min./m³
CYANOSIS,COMA,CONVULSIONS;
RECOVERED IN 10 MIN.
INHALE
EXHALE
START OF EXPOSURE
END OF EXPOSURE
COMA AND CONVULSIONS
7 sec.

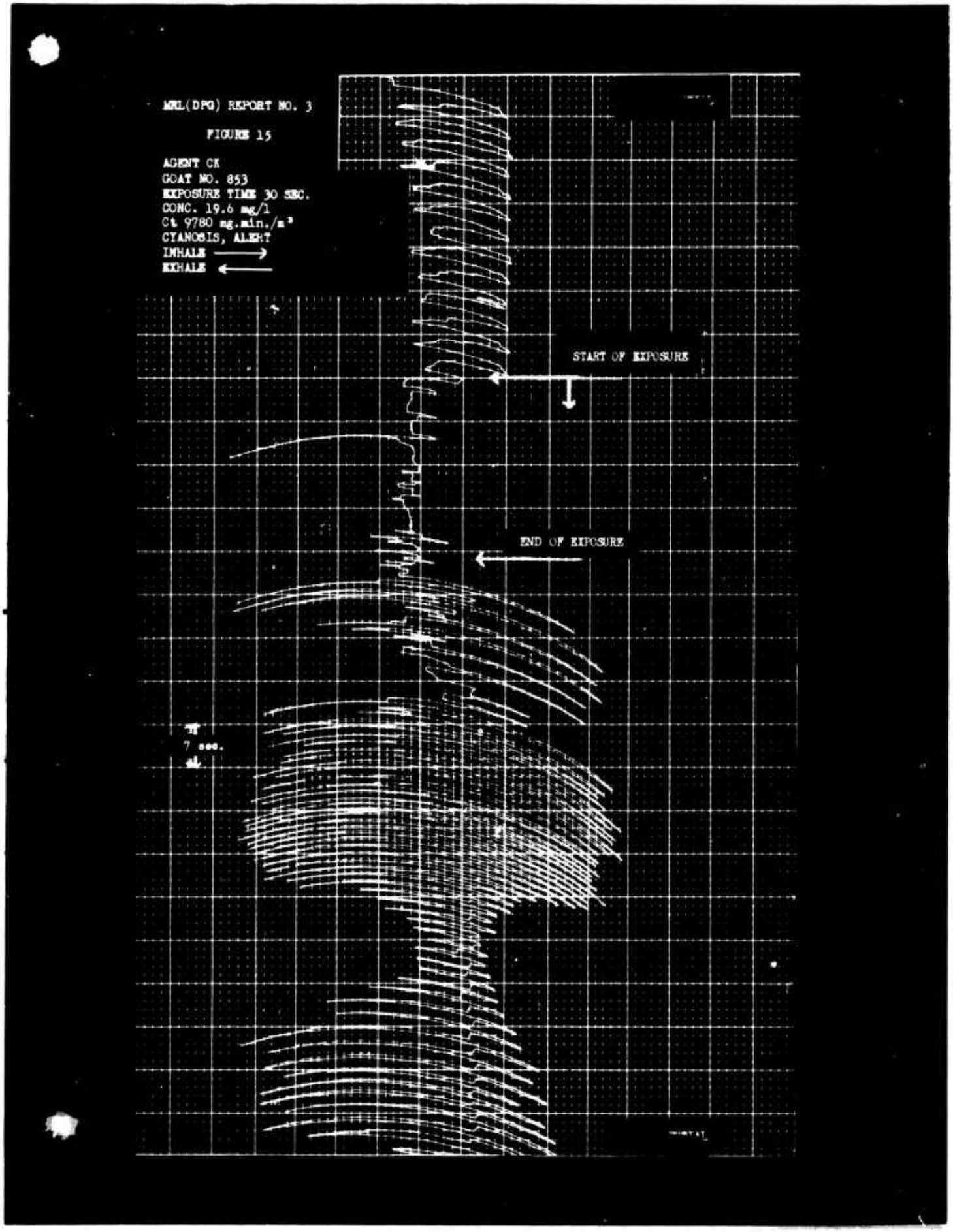

MRL(DPG) REPORT NO. 3
FIGURE 15
AGENT CK
GOAT NO. 853
EXPOSURE TIME 30 SEC.
CONC. 19.6 mg/l
Ct 9780 mg.min./m³
CYANOSIS, ALERT
INHALE
EXHALE
START OF EXPOSURE
END OF EXPOSURE
7 sec.

TABLE X

RESPIRATORY BEHAVIOR OF GOATS EXPOSED TO AC FOR 15 SECONDS

Goat Number	Analytical Concentration	Analytical Ct	Respiratory Behavior: Depressed Phase — Character of Depressed Respiration	Duration	Onset of Stimulation	Onset of Collapse	Time of Death	Recovery Time	Remarks	Figure Number
	Mg./l.	mg.min./m^3		Sec.	Sec.	Sec.	Min.	Min.		
433	45.0	11,250	Shallow	15	15	40	12	--	Pulmonary hemorrhage	20
12	35.5	8,870	Shallow	7	7	45	17	--	Pulmonary hemorrhage	
UNG*	32.7	8,170	Moderate shallow	10	10	30	3	--	Pulmonary hemorrhage	
440	28.4	7,100	Shallow	8	13	40	8	--	Coma and convulsions preceded death	
UNG	27.7	6,930	None	--	15	35	6	--	Coma and convulsions preceded death	
474	27.6	6,900	Shallow	7	7	35	4	--	Coma and convulsions preceded death	
84	27.4	6,850	None	--	7	35	8	--	Coma and convulsions preceded death	
494	26.9	6,720	None	--	18	45	--	30	Convulsions	
812	26.0	6,500	None	--	15	45	--	50	Convulsions	17
575	25.4	6,350	Shallow, 8 sec., breath holding-7 sec.	15	21	None	--	I	No symptoms	22
211	23.0	5,750	Shallow	15	15	60	--	12	Convulsions	
486	20.2	5,050	Shallow, slow	15	15	None	--	I	No symptoms	
35	18.4	4,600	None	--	8	30	7	--	Coma and convulsions preceded death	
143	16.4	4,100	None	--	7	40	7	--	Coma and convulsions preceded death	21
173	14.9	3,720	None	--	8	45	--	30	Convulsions	
305	13.6	3,400	None	--	18	90	--	2	Convulsions	
860	13.0	3,250	None	--	15	40	--	3	Convulsions	

1 - Wearing masks

All times are from start of exposure

I - Immediate Recovery

* Un-numbered Goat

TABLE [illegible]

RESPIRATORY BEHAVIOR OF GOATS[1] EXPOSED TO [illegible] FOR 2 MINUTES AND FOR 30 SECONDS

Goat Number	Time of Exposure	Analytical Concentration	Analytical Ct	Respiratory Behavior: Onset of Stimulation	Respiratory Behavior: Duration of Stimulation	Respiratory Behavior: Onset of Depression	Respiratory Behavior: Onset of Collapse	Response of Goat: Time of Death	Response of Goat: Recovery Time	Remarks	Figure Number
	Min.	mg./l.	mg.min./m^3	Sec.	Sec.	Sec.	Sec.	Min.	Min.		
336	2	8.10	16,200	14	30	44	45	4.5	—	Coma and convulsions preceded death	
537	2	4.71	9,420	22	58	80	80	5	—	Coma and convulsions preceded death	
847	2	4.15	8,300	15	44	59	50	6	—	Coma and convulsions preceded death	
1316	2	2.64	5,280	22	58	80	55	—	27	Convulsions	17
421	2	2.36	4,720	11	62	73	45	5	—	Coma and convulsions preceded death	
200	2	2.32	4,640	25	75	100	85	—	77	Convulsions	
345	2	2.14	4,280	37	71	108	80	10	—	Coma and convulsions preceded death	16
118	2	2.08	4,160	22	57	79	65	4.5	—	Coma and convulsions preceded death	
412	2	1.96	3,920	5	75	80	75	—	52	Convulsions	
UNG	2	1.63	3,260	30	93	123	85	8	—	Coma and Convulsions preceded death	
286	2	1.62	3,240	15	56	71	50	—	52	Convulsions	
305	2	1.24	2,480	59	>135	None	125	—	7	Convulsions	
374	2	1.24	2,480	30	90	120	110	—	22	Convulsions	
603	2	1.10	2,200	24	96	120	73	—	15	Convulsions	
874	2	1.07	2,140	26	100	126	100	—	15	Convulsions	
362	2	0.98	1,960	22	131	153	65	—	38	Convulsions	
197	2	0.89	1,780	38	96	134	140	—	32	Convulsions	
498	2	0.87	1,740	35	78	113	None	—	I	No symptoms	

All times are from start of exposure
I - Immediate recovery
1 - Wearing masks

TABLE XI (Continued)

RESPIRATORY BEHAVIOR OF GOATS[1] EXPOSED TO AC FOR 2 MINUTES AND FOR 30 SECONDS

Goat Number	Time of Exposure	Analytical Concentration	Analytical Ct	Respiratory Behavior: Onset of Stimulation	Respiratory Behavior: Duration of Stimulation	Respiratory Behavior: Onset of Depression	Response of Goat: Onset of Collapse	Response of Goat: Time of Death	Response of Goat: Recovery Time	Remarks	Figure Number
	Min.	Mg./l.	mg. min./m^3	Sec.	Sec.	Sec.	Sec.	Min.	Min.		
439	0.5	15.5	7,750	11	35	46	31	4	—	Coma and convulsions preceded death	
836	0.5	14.9	7,450	8	36	44	30	3.5	—	Coma and convulsions preceded death	
871	0.5	8.9	4,450	17	60	77	60	6.5	—	Coma and convulsions preceded death	
378	0.5	7.3	3,650	13	43	56	45	5.5	--	Coma and convulsions preceded death	18
581	0.5	6.7	3,350	31	>180	None	None	—	I	No symptoms	19
111	0.5	6.6	3,300	20	60	80	60	—	20	Convulsions	
531	0.5	6.3	3,150	30	>150	None	None	—	I	No symptoms	
UNG	0.5	5.9	2,950	7	35	42	58	18	—	Pulmonary hemorrhage	
632	0.5	5.3	2,650	15	>180	None	55	—	11	Convulsions	
81	0.5	4.2	2,100	30	>150	None	70	—	2	Convulsions	

All times are from start of exposure.
I - Immediate recovery.
1 - Wearing masks

CONCLUSIONS
19

[redacted]

Depressed respiration occurred from the onset of exposure in 8 of 12 goats exposed to concentrations over 18.4 mg./l. It was characterized by complete breath holding in one goat and very shallow, slow respiration in the others. This phase continued for 7 to 15 seconds after initial exposure and was immediately followed by stimulated respiration. Respiratory depression as described above followed the stimulated phase. All goats exposed for 15 seconds to concentrations of 27.4 mg./l. or higher died regardless of the nature of their respiration during exposure. Representative tracings of the respiratory pattern for goats exposed to AC are presented in Figures 16 to 22.

4. Toxicity for Exposures of "Masked" Goats.

From the results of studies on respiratory behavior it was possible to estimate the toxicity of CG,CK, and AC for short exposures of goats wearing the special mask. Since a relatively small number of animals were exposed, the values can be considered as only approximate. The following L(Ct)50's were obtained graphically.

Agent	Time of Exposure	No. Goats Exposed	Approximate L(Ct)50 mg.min./m^3
CG	Variable*; average 100 seconds	17	17,000
CK	Two minutes	24	14,000
AC	15 Seconds	17	6,000
AC	30 Seconds	10	3,000
AC	Two minutes	18	4,000

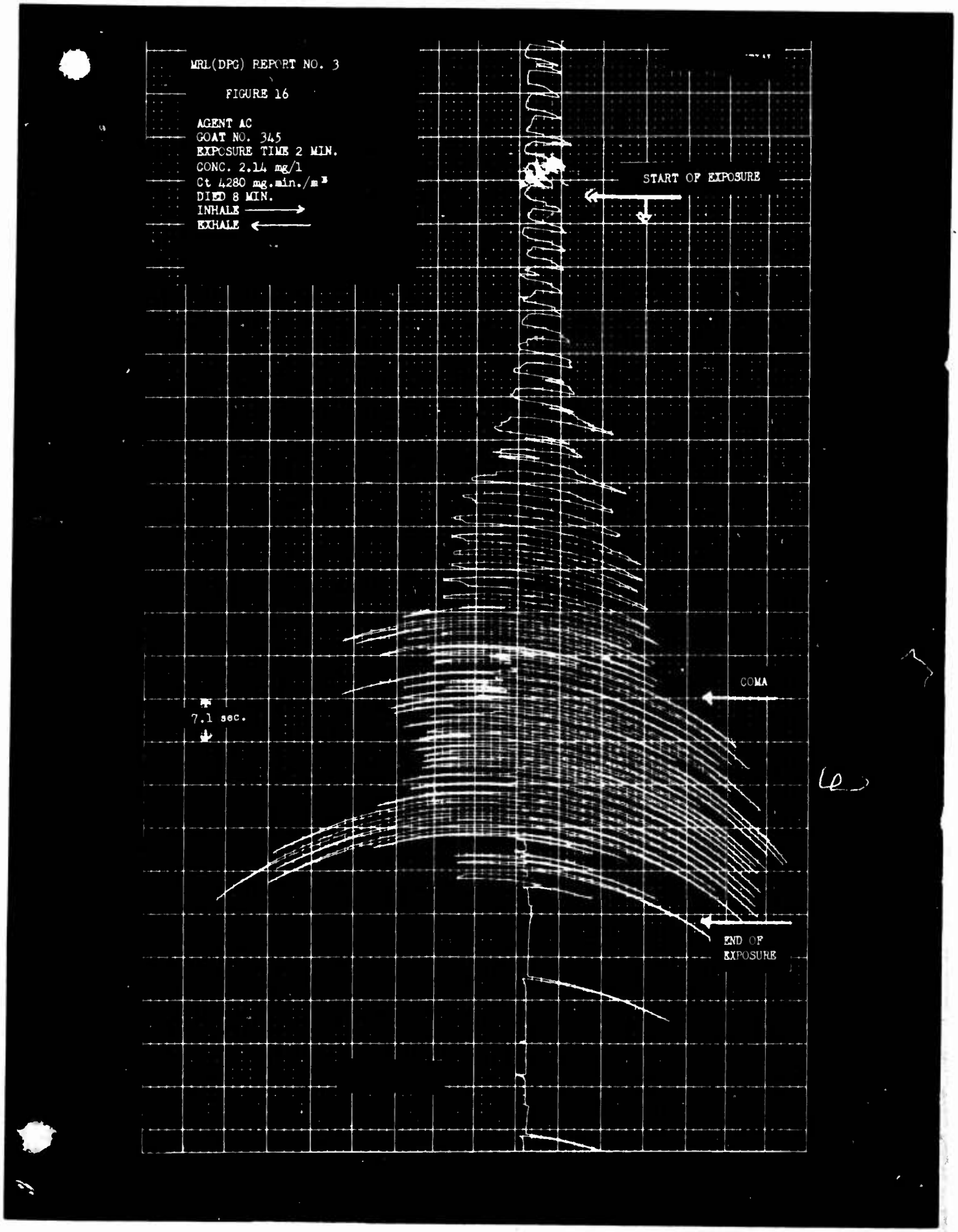
* Results of 330 and 720 second exposures were not included.

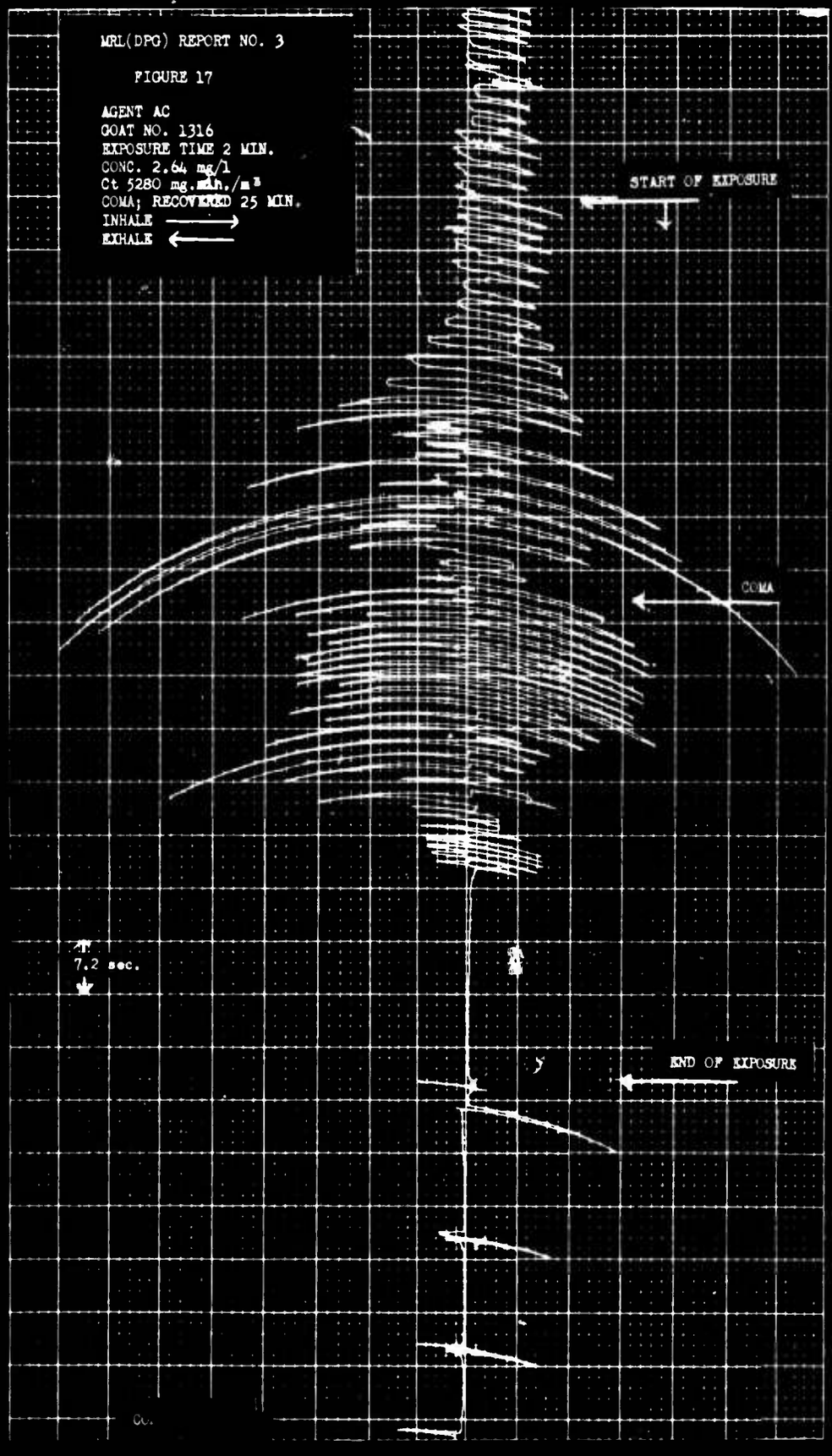
Thirty second exposures to CG and CK showed no correlation between concentration and mortality (7 and 18 goats exposed, respectively). Use of a greater number of animals would not be expected to change this conclusion, since breath holding of 30 seconds duration or longer occurred in 20 out of 21 goats for CG concentrations of 1.3 mg./l. and higher; and since 31 out of 34 goats exposed to CK concentrations of 2.4 mg./l. and higher exhibited respiratory depression for 25 seconds or longer. For each of the three agents studied individual respiratory behavior accounted for every pronounced variation from the plotted log dosage-mortality probit curve.

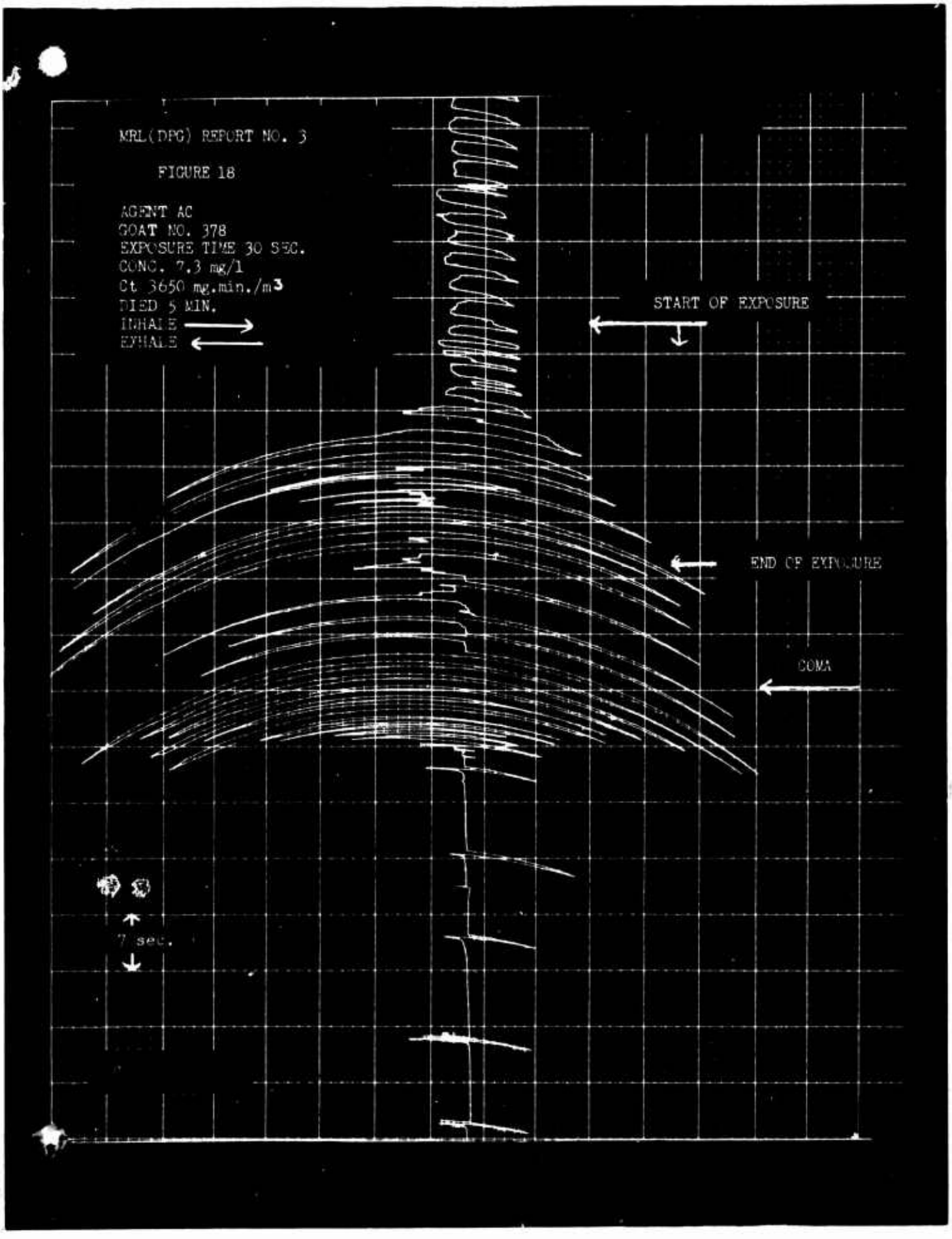
In order to evaluate the effects of skin absorption of AC during short total exposures, six "masked" goats were placed in the chamber for 30 seconds and the chamber atmosphere circulated through the mask at 34 l./min. No significant difference was found between the effects on these "masked" goats and "masked" goats placed outside the chamber (Table XII).

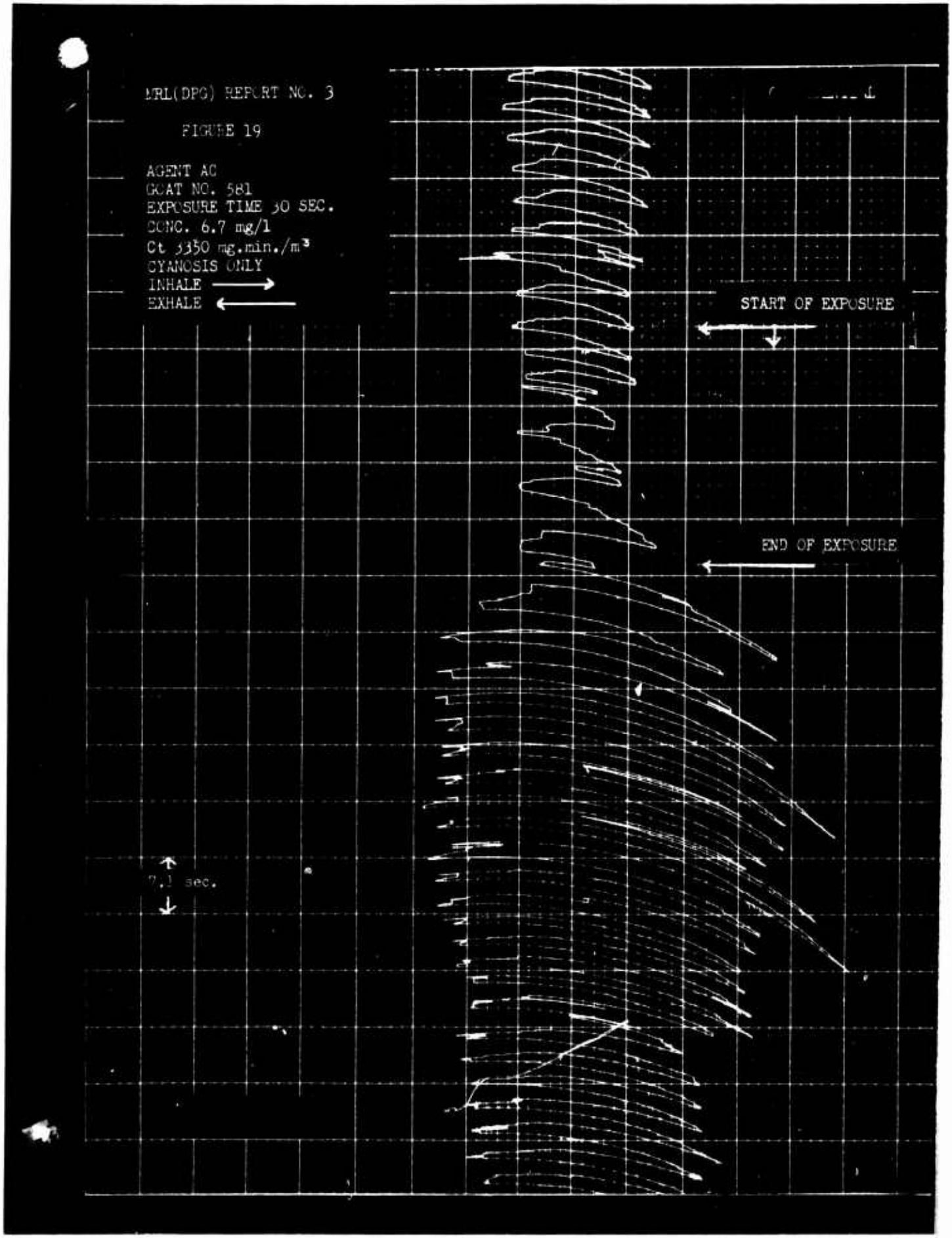
Eleven additional goats with their mouths taped shut to simulate the effect of the mask were placed in the chamber and exposed to AC for 30 seconds. In this manner possible absorption of agent through the mucous membranes of the mouth was eliminated. The approximate L(Ct)50 for these goats was 1700 mg.min./m^3. The details are presented in Table XII.

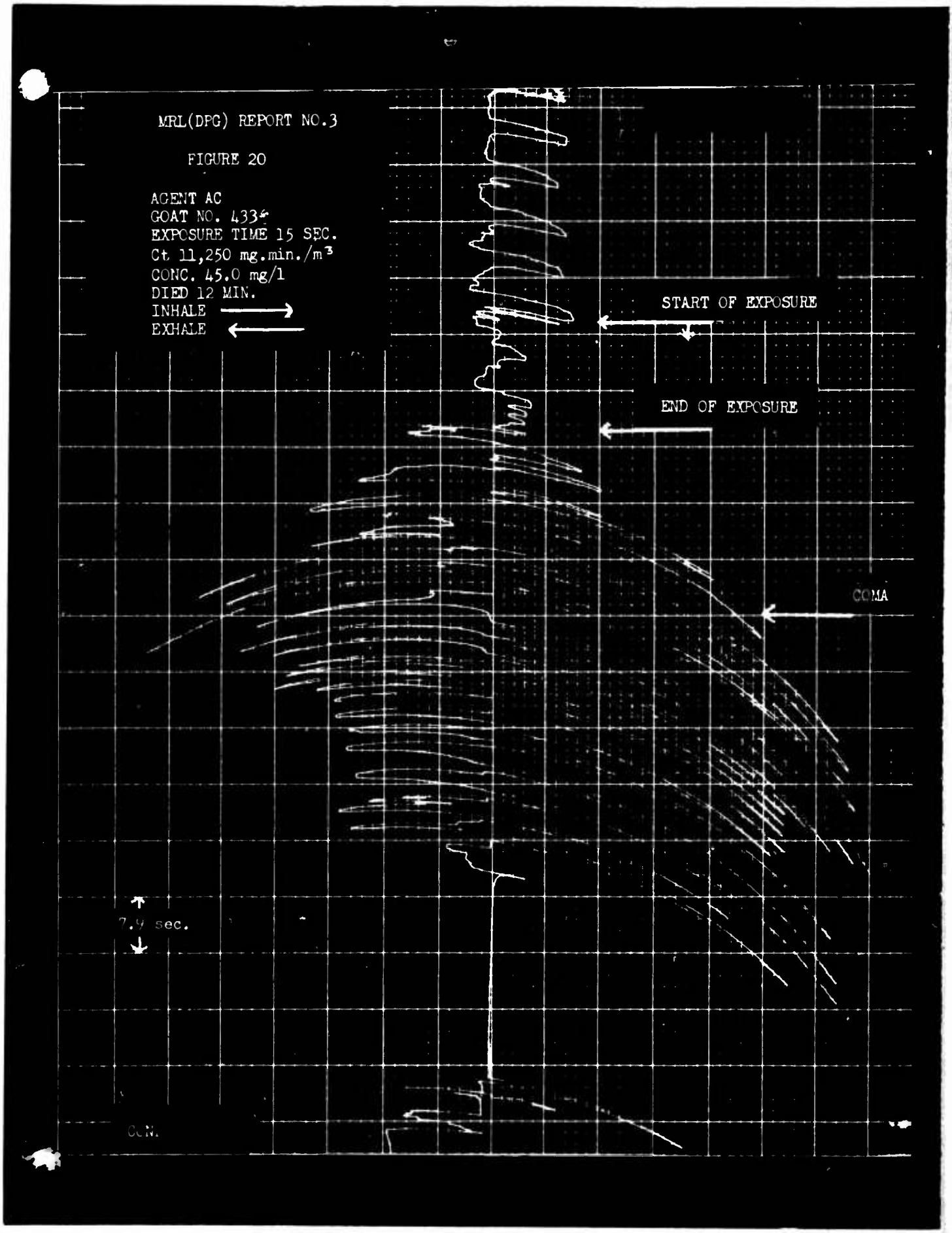
[redacted]

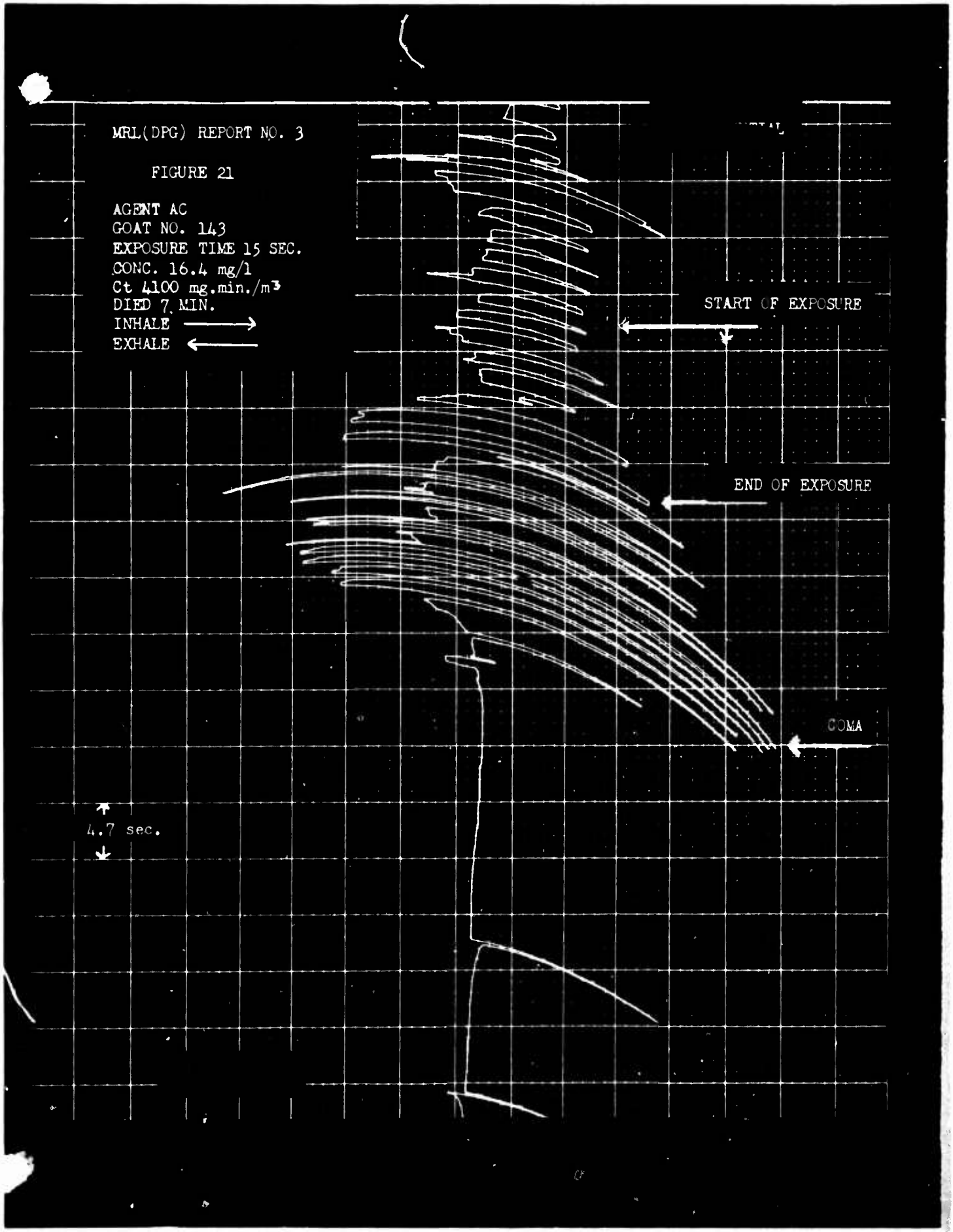

MRL(DPG) REPORT NO. 3
FIGURE 16
AGENT AC
GOAT NO. 345
EXPOSURE TIME 2 MIN.
CONC. 2.14 mg/l
Ct 4280 mg.min./m³
DIED 8 MIN.
INHALE
EXHALE
START OF EXPOSURE
COMA
7.1 sec.
END OF EXPOSURE


MRL(DPG) REPORT NO. 3
FIGURE 17
AGENT AC
GOAT NO. 1316
EXPOSURE TIME 2 MIN.
CONC. 2.64 mg/l
Ct 5280 mg.min./m³
COMA; RECOVERED 25 MIN.
INHALE
EXHALE
START OF EXPOSURE
COMA
7.2 sec.
END OF EXPOSURE


MRL(DPG) REPORT NO. 3
FIGURE 18
AGENT AC
GOAT NO. 378
EXPOSURE TIME 30 SEC.
CONC. 7.3 mg/l
Ct 3650 mg.min./m3
DIED 5 MIN.
INHALE
EXHALE
START OF EXPOSURE
END OF EXPOSURE
COMA
7 sec.


MRL(DPG) REPORT NO. 3
FIGURE 19
AGENT AC
GOAT NO. 581
EXPOSURE TIME 30 SEC.
CONC. 6.7 mg/l
Ct 3350 mg.min./m³
CYANOSIS ONLY
INHALE
EXHALE
START OF EXPOSURE
END OF EXPOSURE
7.1 sec.


MRL(DPG) REPORT NO.3
FIGURE 20
AGENT AC
GOAT NO. 433
EXPOSURE TIME 15 SEC.
Ct 11,250 mg.min./m³
CONC. 45.0 mg/l
DIED 12 MIN.
INHALE
EXHALE
START OF EXPOSURE
END OF EXPOSURE
COMA
7.4 sec.
ECG


MRL(DPG) REPORT NO. 3
FIGURE 21
AGENT AC
GOAT NO. 143
EXPOSURE TIME 15 SEC.
CONC. 16.4 mg/l
Ct 4100 mg.min./m³
DIED 7 MIN.
INHALE
EXHALE
START OF EXPOSURE
END OF EXPOSURE
COMA
4.7 sec.

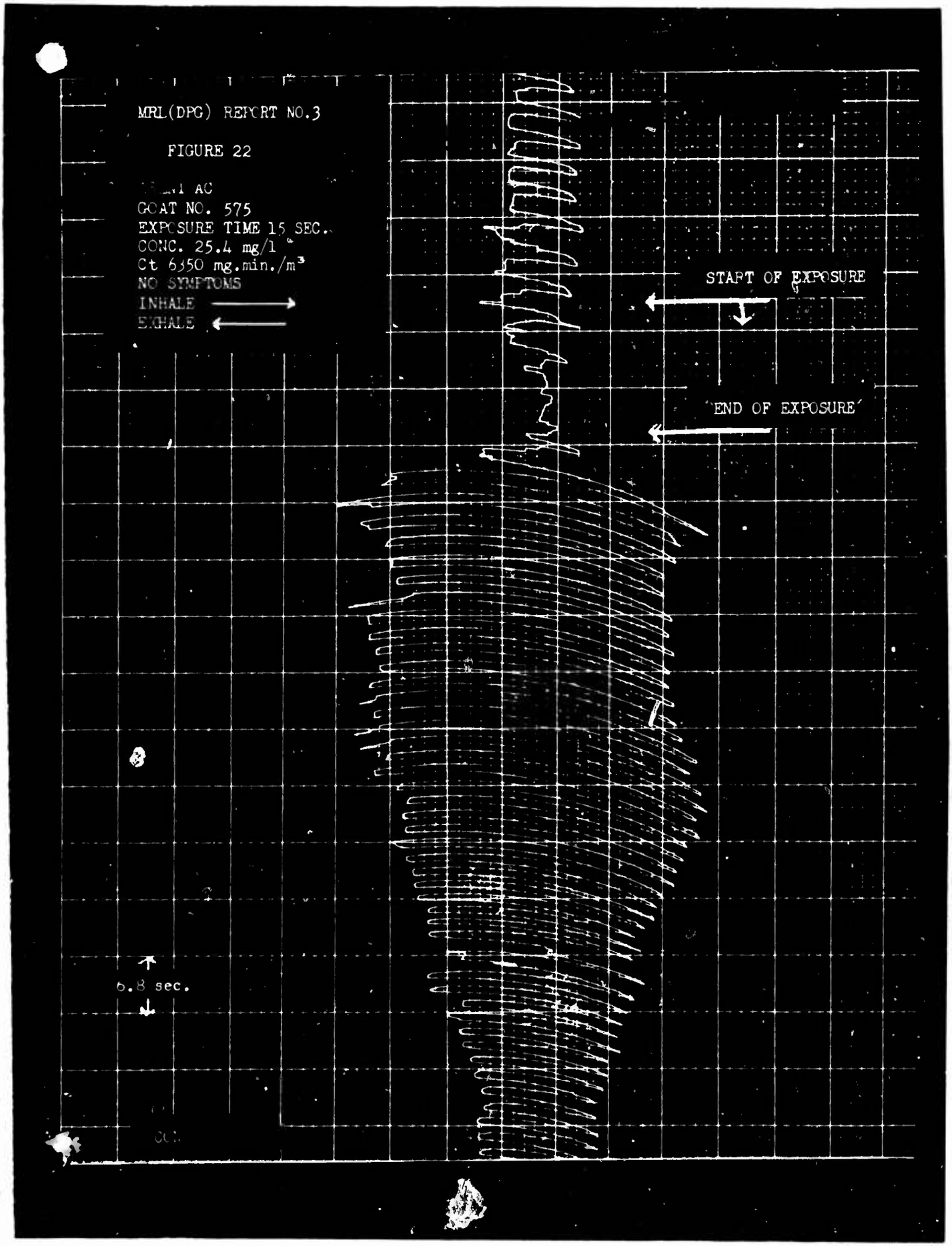

MRL(DPG) REPORT NO.3
FIGURE 22
GOAT NO. 575
EXPOSURE TIME 15 SEC.
CONC. 25.4 mg/l
Ct 6350 mg.min./m³
NO SYMPTOMS
INHALE
EXHALE
START OF EXPOSURE
END OF EXPOSURE
6.8 sec.

TABLE XII

EFFECT OF CLOSING MOUTH OF GOATS EXPOSED TO AC FOR 30 SECONDS

Goat Number	Method of Closing Mouth	Analytical Concentration mg./l.	Analytical Ct mg. min./m³	Time of Collapse Sec.	Time of Death Min.	Time of Recovery Min.	Remarks
							Chamber Gas Drawn Through Mask at 34 l./min. Goat Inside Chamber
42	Masked	5.10	2550	45	—	50	Coma, convulsions
389	Masked	4.57	2285	62	—	2	Cyanosis only
428	Masked	4.37	2185	40	30	—	Epistaxis
1307	Masked	4.27	2135	45	—	8	Coma, convulsions
167	Masked	2.69	1345	50	—	3	Cyanosis only
108	Masked	2.64	1320	40	—	2	Coma, convulsions
							Mouth of Goat Taped Shut. Exposure Made in the Gas Chamber
8	Taped	4.04	2020	25	9	—	Coma and convulsions preceded death
UNG	Taped	4.04	2020	25	—	90	Coma, convulsions
1339	Taped	3.49	1745	41	30	—	Coma and convulsions preceded death
806	Taped	3.49	1745	35	—	9	Coma, convulsions
306	Taped	3.32	1660	45	—	23	Coma, convulsions
398	Taped	3.32	1660	35	—	60	Coma, convulsions
79	Taped	3.32	1660	44	—	6	Coma, convulsions
429	Taped	3.32	1660	37	—	8	Coma, convulsions
292	Taped	3.27	1635	35	15	—	Coma and convulsions preceded death
303	Taped	3.27	1635	35	15	—	Coma and convulsions preceded death
70	Taped	2.24	1120	45	—	5	Coma, convulsions

[redacted]

IV. DISCUSSION.

A. Determination of Toxicity of Nonpersistent Agents for Short Exposures.

It is evident from these and other studies that the toxicity of nonpersistent agents is largely dependent upon the respiratory behavior of the subject during exposure. This is particularly true for short exposures; while in longer exposures (~5 min.) the effects due to initial changes of breathing assume decreasing importance. Because of differences in respiratory response to widely varying concentrations of CG, CK, and AC, it is likely that the log dosage-mortality probit relationships will not always be linear (e.g. 30 second CG exposures), and the L(Ct)50 value will not have its usual significance. For this reason it is most important that determinations of toxicity for short period exposures to these agents include a wide range of concentrations. Omission of the extremes has misled investigators, and has resulted in a misinterpretation of data. The individual differences in respiratory response of the animals, particularly to the irritant gases, CG and CK, often result in unusually wide dispersion of the mortality data. In these cases a determination of L(Ct)50 may be impractical.

The apparent failure of the L(Ct)50's of all of these agents to comply with Haber's Ct law can be accounted for by the respiratory behavior. Extremely high values found for short period exposures to CG and CK are due to respiratory depression during the initial part of the exposure. It is also evident that the relationship of the L(Ct)50 values for "masked" goats for 15 second, 30 second, and 2 minute exposures to AC cannot be fully accounted for by the usual equations (T.D.M.R. 699; Medical Division Report No. 22) taking detoxication into account. The value of 6,000 mg.min./m^3 for 15 second exposures is high because respiratory stimulation does not usually occur during that period. For 30 second and 2 minute exposures lower values of 3000 and 4000 mg.min./m^3 are found because respiratory stimulation during that period results in a much higher respiratory volume.

B. Use of "Masked" Goats.

It is apparent that the toxicity figures for exposures of "masked" and unmasked goats are not in agreement. In each case where a comparison is afforded the L(Ct)50 values for "masked" goats are about two times greater. These are shown as follow:

Agent	Time of Exposure min.	L(Ct)50 for Unmasked Goats mg.min./m^3	Approximate L(Ct)50 for "Masked" Goats mg.min./m^3
CG	2	6500 ± 750	17,000*
CK	2	7000 ± 750	14,000
AC	1/2	1300	3,000
AC	2	2200**	4,000

* t = 45 to 169 seconds, average 100 seconds

** T.R.L.R. 23

[redacted]

It was found that total exposures of goats with their mouths bound shut resulted in slightly increased resistance to AC (approximate L(Ct)50 1700 mg.min./m^3) when compared with total exposures of unmasked goats (L(Ct)50 1300 mg.min./m^3). This increase was less in degree than for total exposures of "masked" goats with the chamber atmosphere circulating through the mask (Table XII).

Several possible sources were considered for this difference in toxicity. Possible dilution of the mask concentration by exhaled air was not thought to be a significant factor because of the rapid circulation rate used through the mask and because, in the case of CK, mask concentrations were found to vary by less than 10% from that of the chamber(Table I) Body absorption was shown not to be an important factor for short exposures It was observed that unmasked goats frequently opened their mouths and licked their lips during exposure, whereas "masked" goats were unable to open their mouths. This could permit additional absorption of agent, particularly AC, through the mucous membrane of the mouth of unmasked goats. However, since the ratios of toxicities are identical(i.e. about 2 for each agent), it seems likely that the differences are caused by a similar factor for each agent. Mouth absorption for AC would therefore appear to be of minor importance. In view of all these observations, it seems most likely that the mask to some degree discourages the breathing effort of the goat. This would result in a decrease in the respiratory minute volume and,consequently, a decreased amount of agent inspired by the animals. There is, however, no reason to believe that the qualitative picture of respiratory behavior of the goat is essentially changed by the mask.

As a result of this investigation it is apparent that the use of "masked" goats for field bio-assay is subject to several marked limitations. Exposures of goats for 30 second intervals to the irritant gases yields no useful information. The toxicity data for comparison to field findings of all agents requires correction for the effect of the surprise mask upon the goat. Where this device is used, steps should be taken to reduce or eliminate dead space within the mask to prevent dilution of the inspired air through rebreathing effects.

C. Limitations of Surprise Effects.

Exposure of goats to high concentrations of CK and CG caused marked respiratory depression of variable duration. That reflex action, mediated by the afferent fibers of the vagus nerve, accounts, at least in part, for this effect has been shown on anesthetized dogs (N.D.R.C. Div. 9 Report of U.C.T.L. 9-4-1-15 April 1944). In many cases, the duration of respiratory depression exceeded the presumed period of exposure to a crash concentration so that the amount of gas inhaled by the animal, and hence the effective dosage, was markedly reduced.

AC, on the other hand, appeared non-irritating in concentrations below 20 mg./l. Even above this level, where initial respiratory depression was observed, the amount of agent inhaled in 15 seconds was often enough to produce death. Its non-irritant properties, combined with respiratory stimulation,make AC the biologically preferable standard nonpersistent agent for obtaining surprise effects. Difficulties in its field dispersal however, reduce its usefulness at the present time.

The data herein presented emphasize the importance of non-irritancy in the use of respiratory lethal agents where surprise is sought.

V. CONCLUSIONS.

A. The toxicity of nonpersistent agents during short exposures is largely dependent on the respiratory response of the subject during exposure.

B. Exposures to high concentrations of the irritant gases, CG and CK, result in reflex respiratory depression. This respiratory depression reduces the effectiveness of crash concentrations of these agents for surprise effects.

C. On the basis of physiological response, AC is the most desirable standard nonpersistent agent for surprise effects.

D. Short interval exposures of "masked" goats to a nonpersistent gas cloud are subject to the following limitations:

1. The effectiveness of the agent is reduced approximately one-half by the presence of the mask under the conditions tested.

2. The dead space of the mask dilutes the agent, unless measures are taken to circulate the atmosphere through the mask.

3. Exposures to irritant gases of two minutes duration or less result in marked variation in response.

4. Exposures to irritant gases of 30 seconds duration or less show no correlation between the concentration of agent and mortality.

VI. RECOMMENDATIONS.

A. Field requirements for non-persistent agents should be re-examined in the light of these results to establish new criteria for lethal surprise effects.

B. New methods for controlled short exposures of goats in the field to nonpersistent agents should be investigated.

C. Field data obtained with unmasked and "masked" goats should be re-evaluated.

[redacted] UNCLASSIFIED

MRL (DPG) REPORT NO. 3
A STUDY OF SHORT INTERVAL EXPOSURES OF GOATS TO CG, CK, AND AC

Experimental Work:
Started: 15 November 1944
Completed: 10 September 1945
Notebooks on file in MRL, DPG

Submitted by:

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US ARMY RESEARCH, DEVELOPMENT AND ENGINEERING COMMAND
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REPLY TO
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MEMORANDUM THRU Director, Edgewood Chemical Biological Center, (RDCB-D/Mr. Joseph Wienand), 5183 Blackhawk Road, Aberdeen Proving Ground, Maryland 21010-5424

FOR Defense Technical Information Center, 8725 John J. Kingman Road, Ft Belvoir, VA 22060

SUBJECT: Internal Request for Change in Distribution

1. This action is in response to an Edgewood Chemical Biological Center (ECBC) Internal Request for a Change in Distribution on documents related to cyanogen chloride.

2. The listed documents in the attachment have been reviewed by ECBC Subject Matter Experts and deemed suitable for the change in distribution to read "Approved for Public Release; distribution unlimited."

3. The point of contact is Adana L. Eilo, ECBC Security Specialist, (410) 436-2063, adana.l.eilo.civ@mail.mil.

Encl

MATTHEW A. SPAULDING
Security Manager

Cyanogen Chloride References

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